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(54) Title: COMPOSITIONS AND METHODS FOR MODULATING A CYTOTOXIC T LYMPHOCYTE IMMUNE RESPONSE

(57) Abstract: The present invention provides compositions and methods for the treatment and prevention of immune disorders.

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# COMPOSITIONS AND METHODS FOR MODULATING A CYTOTOXIC T LYMPHOCYTE IMMUNE RESPONSE

## Related Applications

This application claims the benefit of U.S. Provisional Application Serial No. 60/392,718, filed June 27, 2002, the entire contents of which are incorporated herein by this reference.

## Background of the Invention

The initiation of an immune response against a specific antigen in mammals is brought about by the presentation of that antigen to T lymphocytes. An antigen is presented to T lymphocytes in the context of a major histocompatablity (MHC) complex (also referred to as HLA in humans and H-2 in mice). The three-dimensional structure of the MHC includes a groove or cleft into which the presented antigen fits. When an appropriate receptor on a T lymphocyte interacts with the MHC/antigen complex on an APC in the presence of necessary co-stimulatory signals, the T lymphocyte is stimulated, triggering various aspects of the well characterized cascade of immune system activation events, including induction of cytotoxic T lymphocyte (CTL) function, induction of B lymphocyte function and stimulation of cytokine production (see, *e.g.* Roitt, I and Delves, P. Roitt's Essential Immunology, 10th Ed., Boston, Blackwell Science, 2002; Abbas, A. *et al.* Cellular and Molecular Immunology, W.B. Saunders Company, Philadelphia, 1991; Silverstein, A. A History of Immunology, San Diego, Academic Press, 1989).

There are two basic classes of MHC molecules in mammals, MHC Class I and MHC Class II. Both classes are large complexes formed by association of two separate proteins. MHC Class I molecules present antigen to CD8-positive T lymphocytes, which then become activated and can kill the antigen presenting cell directly. Class I MHC molecules generally receive peptides from endogenously synthesized proteins, such as an infectious virus, in the endoplasmic reticulum at around the time of their synthesis (see, *e.g.*, Williams, A. *et al.* (2002) *Tissue Antigens* 59:3; Konig, R. (2002) *Curr. Opin. Immunol.* 14:75; Anfossi, N. *et al.* (2001) *Immunol. Rev.* 14:75; Gao G. and Jakobsen B (2000) *Immunol. Today* 21:630; Watts,

C and Powis, S. (1999) *Rev. Immunogenet.* 1:60 and Natarajan, K. *et al.* (1999) *Rev. Immunogenet.* 1:32).

MHC Class II molecules present antigen to CD4-positive T helper lymphocytes (Th cells). Once activated, Th cells contribute to the activation of CTLs and B lymphocytes via physical contact and cytokine release. Unlike MHC Class I molecules, MHC class II molecules bind exogenous antigens which have been internalized via non-specific or specific endocytosis. Around the time of synthesis, MHC Class II molecules are blocked from binding endogenous antigen, and instead bind the invariant chain protein (Ii). These MHC Class II-Ii protein complexes are transported from the endoplasmic reticulum to a post-Golgi compartment where Ii is released by proteolysis and exogenous antigenic peptides are bound (see, *e.g.*, Villadangos, J. (2001) *Mol. Immunol.* 38:329; Alfonso, C. and Karlsson, L. (2000) *Ann. Rev. Immunol.* 18:113; Viret, C. and Janeway Jr., C. (1999) *Rev. Immunogenet.* 1:91; Diabata *et al.* (1994) *Molecular Immunology* 31:255 and Xu *et al.* (1994) *Molecular Immunology* 31:723).

MHC Class I and MHC Class II molecules have a distinct distribution among cells. Almost all nucleated cells express MHC Class I molecules, although the level of expression varies between cell types. Cells of the immune system express abundant MHC Class I on their surfaces, while liver cells express relatively low levels. Non-nucleated cells express little or no MHC Class I. MHC Class II molecules are highly expressed on B lymphocytes, dendritic cells and macrophages, but not on other tissue cells. However, many other cell types can be induced to express MHC Class II molecules by exposure to cytokines (see, *e.g.* Roitt, I and Delves, P. Roitt's Essential Immunology, 10th Ed., Boston, Blackwell Science, 2002; Abbas, A. *et al.* Cellular and Molecular Immunology, W.B. Saunders Company, Philadelphia, 1991; Silverstein, A. A History of Immunology, San Diego, Academic Press, 1989).

Cytotoxic T lymphocytes (CTLs) are restricted in their activity by recognizing a specific histocompatability complex (MHC) antigen on the surface of the target cell, as well as a peptide bound in a cleft of the MHC antigen. The foreign antigen may be present as a result of transplantation from an allogeneic host, viral or bacterial infection, mutation, neoplasia, or the like. The involvement of the MHC protein appears to be essential to the attack by CTLs against the cell which includes the

foreign antigen. By monitoring the presence of foreign antigens, the CTLs are able to destroy cells, which if otherwise allowed to proliferate, might result in the proliferation of pathogens or neoplastic cells (see, *e.g.* Roitt, I and Delves, P. Roitt's Essential Immunology, 10th Ed., Boston, Blackwell Science, 2002; Rhodes, D. and Trowsdale, J. (1999) Rev. Immunogenet. 1:21; and Yu, C. (1998) Exp. Clin. Immunogenet. 15:213).

The unique capability of CTLs to kill infected and/or cancerous cells has led researchers to try and develop strategies for using CTLs in the designing of vaccines for the treatment of diseases, *i.e.* pathogenic infections and cancer. However, vaccines of killed pathogens or soluble proteins are not effective in the induction of the CTL response. Moreover, naked DNA, live vectors and attenuated viruses, which are effective CTL inducers, are genetic material and potentially pose a serious health hazard, especially in the case of viruses such as human immunodeficiency virus (HIV) and Ebola virus (see, *e.g.*, Baba, T. *et al.* (1999) *Nat. Med.* 5:194).

This problem was thought to be solved with the finding that specific T-cell epitopes could be synthetically designed and produced. Townsend *et al.* demonstrated that epitopes of influenza nucleoprotein could be defined by short synthetic peptides and thus included in potential vaccine candidates (Townsend, A. *et al.* (1986) *Nature* 324:575). However, success using synthetic peptides has been limited. Documented cases that describe the use of synthetic peptides, relating to influenza, Sendai and lymphocyte choriomeningitis viruses, for use in the *in vivo* priming of CTLs have presented many problems (see, *e.g.*, Kast, W. *et al.*, (1991) Immunol. Lett. 30:229; Aichele, P. *et al.*, (1990) J. Exp. Med. 171:1815; Deres, K. *et al.* (1989) Nature 342:561). In each of the above cases, the immunization protocols proved to be cumbersome, requiring either modifications of peptides or multiple immunizations to demonstrate CTL activity, and difficulty in rapidly screening large numbers of candidate substances.

Moreover, the use of single epitopic peptides has been shown to only generate CTL responses in a small group of individuals, *i.e.* those individuals who have matched MHC antigens, thus decreasing the effectiveness and usefulness of the vaccine. Although the use of multiple epitopic peptides has been shown to increase the size of the population who will benefit from the vaccine (Hanke, T and McMichael, A. (2000) *Nat. Med.* 6:951), it remains difficult and labor intensive to

accurately predict from a sequence of an antigenic protein how the protein will be processed and which peptide portions will bind HLA class I molecules and be presented to CTLs.

The present invention provides an effective method of modulating, *e.g.*, inducing, an immune response, *e.g.*, a CTL-mediated immune response, which avoids may of the problems associated with the previously suggested methods. Specifically, the present invention allows for the development of vaccines that are capable of inducing antigen-specific immune responses in subjects of varying genetic backgrounds without the labor intensive task of determining immunostimulatory epitopes.

## Summary of the Invention

The present invention provides, at least in part, methods and compositions for the treatment of immune disorders, such as, for example, viral, bacterial and parasitic infections, prion diseases, neoplastic diseases and protection against toxins. The invention is based on the discovery that overlapping synthetic peptide formulations (OSPFs) of the present invention are able to modulate, *e.g.*, induce, immune responses, such as cytotoxic T lymphocyte (CTL)-mediated response and antibody-associated immune responses, thus indicating a wide applicability for human and veterinary applications.

Accordingly, the present invention provides a method of modulating, *e.g.* inducing, an immune response by administering to a subject, *e.g.*, a vertebrate, such as a human, an effective amount of an OSPF. The OSPF of the present invention includes a combination of single chain peptides that correspond to an amino acid sequence of a protein of interest, such that the single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1), and X represents the number of amino acids of the protein of interest, where at least 1 single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1), such that the length of the single chain peptide is able to be internalized by, *e.g.*, phagocytosis, receptor-mediated endocytosis, and the like, by a MHC bearing cell, *i.e.*, a MHC class I- or MHC class II-bearing cell, and be presented by an MHC molecule to a T cell.

In another embodiment, the OSPFs of the present invention are not overlapping, but instead are adjoining. Therefore, in this embodiment, the OSPF of the present invention includes a combination of single chain peptides that correspond to an amino acid sequence of a protein of interest, such that the single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and X represents the number of amino acids of the protein of interest, such that the length of the single chain peptide is able to be internalized, *e.g.*, phagocytosis, receptor-mediated endocytosis, and the like, by a MHC-bearing cell, *i.e.* a MHC Class I- or MHC Class II-bearing cell, and be presented by an MHC molecule to a T cell.

In one embodiment, the immune response is a Th1-mediated immune response, such as a CTL-mediated immune response. In another embodiment, the immune response is a Th2-mediated immune response, such as an antibody-associated immune response.

In one embodiment, Y is at least 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 amino acids.

In another embodiment, Z is at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29 amino acids.

In other aspects, the invention pertains to a method of treating or preventing an OSPF-associated disorder in a subject. The method includes administering to the subject an effective amount of an OSPF of the present invention, thereby treating or preventing the OSPF-associated disorder in the subject. By "OSPF-associated disorder" is meant any disease, disorder or condition which can be treated or prevented through the modulation of an immune response. Examples of OSPF-associated disorders include, but is not limited to, viral infections due to viruses (*e.g.*, Ebola virus, hepatitis C, HIV, *e.g.*, HIV-1 and HIV-2, RSV, monkeypox, and SARS coronavirus, bacterial infections due to bacteria (*e.g.*, anthrax, Listeria monocytogenes, Legionella and mycobacterium such as tuberculosis), parasitic infections (*e.g.* malaria), protection against toxins (*e.g.*, shigella toxin, toxin botulinum and tetanus toxin), parasitic infections due to parasites (*e.g.*, Plasmodium, Trypanosoma, Schistosoma and Toxoplasmosis), prions and neoplastic diseases (*e.g.*, breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal (*e.g.*, pancreatic and stomach) cancer and osteogenic sarcoma).

In yet another embodiment, the protein of interest can be any protein associated with an OSPF-associated disorder, including, but not limited to, HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235). For example, OSPFs for HIV-1 Gag include the peptides set forth as SEQ ID NO:1-122 and/or SEQ ID NO:236-335 and OSPFs for SIV Envelope protein include the peptides set forth as SEQ ID NO:123-206 and/or 336-338.

In another aspect, the invention provides a vaccine for immunizing a subject against an OSPF-associated disorder, wherein the vaccine comprises an OSPF of the present invention and a pharmaceutically-acceptable carrier. In another aspect, the invention provides a pharmaceutical composition comprising an OSPF of the present invention and a pharmaceutically acceptable carrier. In yet another aspect, the invention features a kit for immunizing a subject against an OSPF-associated disorder, wherein the kit comprises an OSPF of the present invention and may further comprise instructions for use.

In yet another aspect, the invention features a vaccine adjuvant which comprises an OSPF of the present invention and a pharmaceutically acceptable carrier which may be used to enhance the efficacy of a vaccine.

## Brief Description of the Drawings

*Figures 1a - 1c* are graphs depicting the CTL activity induced by OSPF-HIV Gag in BALB/c and C57BL/6 mice.

*Figures 2a and 2b* are graphs depicting T cell proliferation induced by OSPF-HIV Gag in BALB/c and C57BL/6 mice

*Figures 3a and3b* are graphs depicting the CTL activity induced by OSPF-SIV *ex vivo* by human dendritic cells and autologous PBMCs, as assessed by ELISPOT™ and $^{51}Cr$ release assays, respectively.

## Detailed Description of the Invention

### *Definitions*

Before further description of the present invention, and in order that the invention may be more readily understood, certain terms are first defined and collected here for convenience.

The term "overlapping synthetic peptide formulation" or "OSPF" refers to a combination of single chain peptides which correspond to an amino acid sequence of a protein of interest, represented by Y, wherein Y is at least 7 to (X-1) and X represents the number of amino acids of the protein interest where at least 1 single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1). The length of the single chain peptide must be such that internalization, *e.g.*, phagocytosis, receptor-mediated endocytosis, and the like, of the single chain peptide by a MHC-bearing cell, *i.e.* a MHC-Class I- or MHC Class II-bearing cell, can occur. Preferably, the cell is a MHC Class I-bearing cell. Furthermore, the OSPF must be of a length to allow presentation by a MHC molecule to a T cell. In certain embodiments, Y is at least 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 amino acids in length. In other

embodiments, the length of Z is at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28 or 29 amino acids.

In another embodiment of the invention, the OSPF refers to a combination of single chain peptides that correspond to a protein of interest and are represented by Y, wherein Y is 1 to (X-1), where X represents the number of amino acids of the protein of interest. The length of the single chain peptide must be such that internalization, *e.g.*, phagocytosis, receptor-mediated endocytosis, and the like, of the single chain peptide by a MHC-bearing cell, *i.e.* a MHC Class I- or MHC Class II-bearing cell, can occur. Furthermore, the OSPF must be of a length to allow presentation by a MHC molecule to a T cell. Preferably, the cell is a MHC Class I-bearing cell. In certain embodiments, Y is at least 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 amino acids in length.

As used herein, the term "combination" or "a combination of" refers to two or more single chain peptides.

The term "peptide" or "single chain peptide" or "polypeptide" is used in its broadest sense, *i.e.*, any polymer of amino acids (dipeptide or greater) linked through peptide bonds. Thus, the term "peptide" includes proteins, oligopeptides, protein fragments, mutants, fusion proteins and the like. The term "protein" is used herein to designate a naturally occurring polypeptide. Peptides of the present invention can be made synthetically, using techniques that are known in the art, or encoded by a nucleic acid, such as DNA or RNA.

The present invention also includes a recombinant molecule comprising a nucleic acid sequence encoding an OSPF(s), operatively linked to a vector capable of being expressed in a host cell. As used herein, "operatively linked" refers to insertion of a nucleic acid sequence into an expression vector in such a manner that the sequence is capable of being expressed when transformed into a host cell. As used herein, an "expression vector" is an RNA or DNA vector capable of transforming a host cell and effecting expression of an appropriate nucleic acid sequence, preferably replicating within the host cell. An expression vector can be either prokaryotic or eukaryotic, and typically is a virus or a plasmid. Suitable host cells can be any cells that are capable of producing the peptides of the present invention. Such host cells include, but are not limited to, bacterial, fungal, insect and mammalian cells. Host cells of the present invention can also be cells which naturally express an MHC

molecule, or are capable of expressing an MHC molecule, and can produce the peptides of the present invention and present them on a MHC molecule. Suitable host cells also include mammalian cells which express MHC molecules on their cell surface and are capable of stimulating an immune response. Examples include, but are not limited to, T cells and antigen presenting cells, such as B cells, dendritic cells, and macrophages. Other examples include non-immune cells which express MHC class I molecules on the cell surface, and include, but are not limited to, fibroblasts, epithelial cells and endothelial cells.

The term "overlapping synthetic peptide formulation (OSPF)-associated disorder" includes any disease, disorder or condition which can be treated or prevented through the modulation, *e.g.*, up-regulation or down-regulation, of an immune response. In certain embodiments, the immune response is a Th-1-mediated immune response, such as a CTL-mediated immune response. In another embodiment, the immune response is a Th2-mediated immune response, such as an antibody-associated immune response. In certain embodiments, OSPF-associated disorders include disorders in which CTL activity is low, aberrant or absent. In other embodiments, the OSPF-associated disorder is an intracellular infection, *e.g.*, a viral infection, a bacterial infection, a parasitic infection, toxic poisoning, prion disease and a neoplastic disease.

The term "protein of interest" refers to any protein associated with an OSPF-associated disorder. Examples of proteins of interest include, but are not limited to, HIV Gag protein (SEQ ID NO:239) SIV Envelope protein (SEQ ID NO:240); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A

(SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235). For example, OSPFs for HIV-1 Gag include the peptides set forth as SEQ ID NO:1-122 and/or SEQ ID NO:236-335 and OSPFs for SIV Envelope protein include the peptides set forth as SEQ ID NO:123-206 and/or 336-338.

The methods of the present invention are effective for preventing, treating or eliminating disease caused by a variety of viruses such as, but not limited to, HIV, *e.g.*, HIV-1 and HIV-2, human herpes viruses, cytomegalovirus (esp. Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, coronaviruses (*e.g.* SARS coronavirus), orthopoxviruses (*e.g.* monkeypox and smallpox), paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18 and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus.

The methods of the present invention are effective for preventing, treating or eliminating disease caused by a variety of bacterial organisms, including gram-positive and gram-negative bacteria. Examples include, but are not limited to, Neisseria spp, including N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H. influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis; Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S.

typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii; Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae. Preferred bacteria include, but are not limited to, Listeria, mycobacteria, mycobacteria (*e.g.*, tuberculosis), Anthrax, Salmonella and Listeria monocytogenes.

The methods of the present invention are effective for preventing, treating or eliminating disease caused by a variety of protozoal and parasitic organisms such as, but not limited to, Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptosporondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse, Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris. The methods are particularly useful for treating blood-borne protozoal and parasitic diseases.

As used herein, the term "state of toxicity" or "toxin-induced condition" refers to the quality of being poisonous, *i.e.* that caused by a poison or toxin. As used in the art, this term also refers to the degree of virulence of a toxic microbe or of a poison. By "toxin" it is meant a poisonous substance of biological origin, which necessarily excludes synthetic toxins which are not encoded by a living organism. The toxins are usually, but are not necessarily, proteins. The methods of the present invention for treating and preventing a toxin-related OSPF disorder are effective for preventing, treating or eliminating toxicity caused by a variety of toxins. Nonlimiting examples of protein toxins include botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin,

aconotoxin, snake venom, scorpion venom and other spider venoms. A nonlimiting example of a non-protein toxin is tricothecene (T-2). Toxin-producing microorganisms of interest include, but are not limited to: Corynebacterium diphtheriae, Staphylococci, Salmonella typhimuium, Shigellae, Pseudomonas aeruginosa, Vibrio cholerae, Clostridium botulinum, and Clostridium tetani. A nonlimiting example of a toxin producing plant is Ricinus communis, and of a fungus producing a toxin is Aspergillus favus.

The methods of the present invention are effective for preventing, treating or eliminating disease caused by prions, such as, but not limited to, familial Creutzfeldt-Jakob disease, Gerstmann-Straussler-Scheinker disease, bovine spongiform encephalopathy (BSE), scrapie and fatal familial Insomnia. As used herein, the term "prion" or "prion disease" refers to a group of transmissible spongiform encephalopathies or TSE. TSEs are caused by abnormalities of the prion protein (PrP). For example, Creutzfeldt-Jakob disease is caused by the conversion of the normal protease-sensitive PrP isoform, designated PrP(C), to a protease resistant isoform, designated PrP(Sc). The change of PrPC into PrPSc can occur spontaneously, however, it can also be induced by PrPSc. PrP(Sc) forms into an infectious particle, named a 'prion' that can transmit the disease. The process by which prions proceed to the central nervous system (CNS) following peripheral uptake is referred to as neuroinvasion Accumulation of PrP(Sc) in the brain causes degenerative disorders affecting the CNS leading to neurodegeneration.

As used herein, the term "neoplastic disease" is characterized by malignant tumor growth or in disease states characterized by benign hyperproliferative and hyperplastic cells. The common medical meaning of the term "neoplasia" refers to "new cell growth" that results as a loss of responsiveness to normal growth controls, *e.g.*, neoplastic cell growth.

As used herein, the terms "hyperproliferative", "hyperplastic", malignant" and "neoplastic" are used interchangeably, and refer to those cells in an abnormal state or condition characterized by rapid proliferation or neoplasia. The terms are meant to include all types of hyperproliferative growth, hyperplastic growth, cancerous growths or oncogenic processes, metastatic tissues or malignantly transformed cells, tissues, or organs, irrespective of histopathologic type or stage of invasiveness. A "hyperplasia" refers to cells undergoing an abnormally high rate of growth. However,

as used herein, the terms neoplasia and hyperplasia can be used interchangeably, as their context will reveal, referring generally to cells experiencing abnormal cell growth rates. Neoplasias and hyperplasias include "tumors," which may be either benign, premalignant or malignant.

The terms "neoplasia," "hyperplasia," and "tumor" are often commonly referred to as "cancer," which is a general name for more than 100 diseases that are characterized by uncontrolled, abnormal growth of cells. Examples of cancer include, but are not limited to: breast; colon; non-small cell lung, head and neck; colorectal; lung; prostate; ovary; renal; melanoma; and gastrointestinal (*e.g.*, pancreatic and stomach) cancer; and osteogenic sarcoma.

The term "tumor antigen" as used herein relates to any antigen expressed on a tumor cell, including but not limited to, Mucin1, carcinoembryonic antigen, oncofetal antigens and tumor-associated antigens. Also included in this definition are any antigens expressed by tumor cells that are encoded by a single DNA strand.

The terms "induce", "inhibit", "potentiate", elevate", "increase" "decrease" or the like, denote quantitative differences between two states, refer to at least statistically significant differences between the two states. For example, "an amount effective to inhibit growth of hyperproliferative cells" means that the rate of growth of the cells will at least statistically significantly different from the untreated cells. Such terms are applied herein to, for example rates of cell proliferation.

As used herein, the term "subject" is intended to include all vertebrates, *i.e.* human and non-human animals. The term "non-human animals" of the invention includes, but is not limited to, mammals, rodents, mice, and non-mammals, such as non-human primates, sheep, dog, horse, cow, chickens, amphibians, reptiles and the like. In one embodiment, the subject is a mammal, *e.g.*, a primate, *e.g.*, a human. In another embodiment, human animals include a human patient suffering from or prone to suffering from an OSPF-associated disorder.

The term "treatment" or "treating" as used herein refers to either (1) the prevention of a disease or disorder (prophylaxis), or (2) the reduction or elimination of symptoms of the disease or disorder (therapy).

The terms "prevention", "prevent" or "preventing" as used herein refers to inhibiting, averting or obviating the onset or progression of a disease or disorder (prophylaxis).

As used herein, the terms "immune" and "immunity" refers to the quality or condition of being able to resist a particular disease.

The terms "immunize" and "immunization," as used herein, refer to the act of making a subject (1) not susceptible to a disease or disorder; or (2) less responsive to a disease or disorder; or (3) have an increased degree of resistance to a disease or disorder.

The term "MHC-bearing cell" refers to any cell which expresses an MHC molecule, *i.e.* MHC Class I or Class II molecule, on the cell surface. In humans, almost all nucleated cells express MHC Class I molecules, although the level of expression varies between cell types. Cells of the immune system express abundant MHC Class I on their surfaces, while liver cells express relatively low levels. MHC Class II molecules are primarily expressed on immune cells, particularly antigen presenting cells, *i.e.*, B cells, dendritic cells, monocytes and macrophages. However, many other cell types can be induced to express MHC Class II molecules and are also meant to be within the scope of the invention. MHC molecules often have different names between vertebrates. For example, MHC is often referred to as HLA in humans and H-2 in mice. These differences in nomenclature are intended to be within the scope of the present invention.

The term "immune cell" includes cells of the immune system which are capable of expressing, producing or secreting cytokines that regulate an immune response, for example a type-1 (Th1) or type-2 (Th2) immune response. Preferred immune cells include human immune cells. Exemplary preferred immune cells include, but are not limited to, macrophages, dendritic cells, T cells, B cells and neutrophils.

As used herein, the term "T cell" (*i.e.* T lymphocytes) is intended to include all cells within the T cell lineage, including thymocytes, immature T cells, mature T cells (including T cells bearing the surface markers CD4 and/or CD8) and the like, from a mammal (*e.g.* human or mouse). Preferably, the T cell is a $CD8^+$ T cell, also referred to herein as a "cytotoxic T lymphocyte" or "CTL", or a $CD4^+$ T cell, also referred to herein as a "helper T lymphocyte" or "Th lymphocyte". MHC Class II molecules present antigen to $CD4^+$ Th cells and once activated, Th cells contribute to the activation of CTLs and B lymphocytes via physical contact and cytokine release.

As used herein, "cytotoxicity" or "induce the killing" of an infected cell or hyperproliferative cell, *e.g.* neoplastic cell, *e.g.* benign hyperplastic cell, refers to the

partial or complete elimination of such cells by a CD8+ T cell (or CTL), and does not necessarily indicate a total elimination of the infection or neoplastic growth.

The term "cytokine" is meant to include any one of the group of hormone-like mediators produced by T and B lymphocytes. Representative cytokines include but are not limited to Interleukin-1 (IL-1), IL2, IL3, IL4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-18, Interferon gamma (IFN-γ), Tumor Necrosis Factor alpha (TNF-α), and Transforming Growth Factor-beta (TGF-β). An "active" fragment of a cytokine is a fragment of a cytokine that retains activity as determined using standard *in vitro* and *in vivo* assays. For example, assays for determining IL2 and IFN-γ activity are known in the art (See *e.g.* Campos, M. (1989) *Cell. Immun.* 120:259-269 and Czarniecki, C. W. (1986) *J. Interferon Res.* 6:29-37.) Assays for determining the activity of other cytokines are known and can readily be conducted by those having ordinary skill in the art.

The term "immune response" includes any response associated with immunity including, but not limited to, increases or decreases in cytokine expression, production or secretion (*e.g.*, IL-12, IL-10, TGFβ or TNFα expression, production or secretion), cytotoxicity, immune cell migration, antibody production and/or immune cellular responses. The phrase "modulating an immune response" or "modulation of an immune response" includes upregulation, potentiating, stimulating, enhancing or increasing an immune response, as defined herein. For example, an immune response can be upregulated, enhanced, stimulated or increased directly by use of a modulator of the present invention (*e.g.*, a stimulatory modulator). Alternatively, a modulator can be used to "potentiate" an immune response, for example, by enhancing, stimulating or increasing immune responsiveness to a stimulatory modulator. The phrase "modulating an immune response" or "modulation of an immune response" also includes downregulation, inhibition or decreasing an immune response as defined herein.

Immune responses in a subject or patient can be further characterized as being either type-1 or type-2 immune responses.

A "type-1 immune response", also referred to herein as a "type-1 response" or a "T helper type 1 (Th1) response" includes a response by $CD4^+$ T cells that is characterized by the expression, production or secretion of one or more type-1 cytokines and that is associated with delayed type hypersensitivity responses. The

phrase "type-1 cytokine" includes a cytokine that is preferentially or exclusively expressed, produced or secreted by a Th1 cell, that favors development of Th1 cells and/or that potentiates, enhances or otherwise mediates delayed type hypersensitivity reactions. Preferred type-1 cytokines include, but are not limited to, GM-CSF, IL-2, IFN-γ, TNF-α, IL-12, IL-15 and IL-18.

Included within a Th1-mediated response is a CTL-mediated immune response. The term "CTL-mediated immune response" includes any response associated with cytotoxic T cell ($CD8^+$ T cell) immunity including, but not limited to, increases or decreases in cytokine expression, production or secretion (*e.g.*, IL-2, IL-12, IL-15, or IFN-γ expression, production or secretion), cytotoxicity, immune cell migration, antibody production and/or immune cellular responses. The phrase "modulating a CTL-mediated immune response" or "modulation of a CTL-mediated immune response" includes upregulation, potentiating, stimulating, enhancing or increasing an immune response, as defined herein. For example, a CTL-mediated immune response can be upregulated, enhanced, stimulated or increased directly by use of an OSPF of the present invention (*e.g.*, a stimulatory modulator). Alternatively, an OSPF can be used to "potentiate" a CTL-mediated immune response, for example, by enhancing, stimulating or increasing immune responsiveness to a stimulatory modulator. The phrase "modulating a CTL-mediated immune response" or "modulation of a CTL-mediated immune response" also includes downregulation, inhibition or decreasing a CTL-mediated immune response as defined herein.

The phrase "type-1 immunity" includes immunity characterized predominantly by type-1 immune responses (*e.g.*, cellular cytotoxicity, delayed type hypersensitivity, and/or macrophage activation), by expression, production or secretion of at least one type-1 cytokine and/or expression of a type-1 immunity cytokine profile. The phrase "potentiating or potentiation of a type-1 or type-2 immune response" includes upregulation, stimulation or enhancement of a type-1 or type-2 response, respectively (*e.g.*, commitment of T helper precursors to either a Th1 or Th2 lineage, further differentiation of cells to either the Th1 or Th2 phenotype and/or continued function of Th1 or Th2 cells during an ongoing immune response). For a review of Th1 and Th2 subsets see, for example, Seder and Paul (1994) *Ann. Rev. Immunol.* 12:635-673.

A "type-2 immune response", also referred to herein as a "type-2 response or a "T helper type 2 (Th2) response" refers to a response by $CD4^+$ T cells that is characterized by the production of one or more type-2 cytokines and that is associated with humoral or antibody-associated immunity (*e.g.*, efficient B cell, "help" provided by Th2 cells, for example, leading to enhanced modification of certain IgG subtypes and/or IgE). The phrase "type-2 cytokine" includes a cytokine that is preferentially or exclusively expressed, produced or secreted by a Th2 cell, that favors development of Th2 cells and/or that potentiates, enhances or otherwise mediates antibody production by B lymphocytes. Preferred type-2 cytokines include, but are not limited to, IL-4, IL-5, IL-6, IL-10, and IL-13.

As used herein, the term "activity", "biological activity" or "functional activity", refers to an activity exerted by a molecule of the invention *e.g.*, an OSPF, as determined *in vivo*, or *in vitro*, according to standard techniques and/or methods such as those described in the Examples.

***Embodiments of the Invention***

The present invention provides, at least in part, methods and compositions for the treatment of immune disorders, such as, for example, viral, bacterial and parasitic infections, prion disease, neoplastic diseases and protection against toxins. The invention is based on the discovery that overlapping synthetic peptide formulations (OSPFs) of the present invention are able to modulate a cytotoxic T lymphocyte (CTL)-mediated response.

Accordingly, the present invention provides a method of modulating, *e.g.* inducing, an immune response, *i.e.*, a Th1-mediated immune response such as a CTL-mediated immune response or a Th2-mediated immune response and an antibody-associated immune response, by administering to a subject, *e.g.*, a vertebrate, such as a human, an effective amount of an OSPF. The OSPF of the present invention includes a combination, *i.e.*, two or more, of single chain peptides that correspond to an amino acid sequence of a protein of interest, such that the single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and where X is the number of amino acids of the protein of interest, and where at least 1 single chain peptide overlaps with another single chain peptide by a length of Z, wherein Z is 1 to (Y-1),

such that the length of the single chain peptide is such that it is able to be internalized by a MHC-bearing cell and can be presented on a MHC molecule to a T cell.

In another embodiment, the OSPF of the present invention includes a combination of single chain peptides that correspond to an amino acid sequence of a protein of interest, such that the single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and where X is the number of amino acids of the protein of interest, such that the length of the single chain peptide is such that it is able to be internalized by a MHC-bearing cell and can be presented on a MHC molecule to a T cell.

In a particular embodiment, Y is at least 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 amino acids.

In another embodiment, the overlap between single chain peptides is at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28 or 29 amino acids.

The invention also includes several variations of an OSPF. Examples include, but are not limited to, an OSPF alone or in combination with other proteins or peptides, *e.g.*, a single set of OSPFs from one protein of interest; two or more OSPFs from the same organism or tumor, but different proteins of interest; different OSPFs from different proteins of interest from different organisms or tumors; a single set of OSPFs from a protein of interest and a killed or attenutated organism; a single set of OSPFs and a tumor-related protein (*i.e.* a tumor antigen); a single set of OSPFs from a protein of interest one or more antibody epitopic peptides; and a single set of OSPFs and one or more Th-related epitopic peptides.

The number of single chain peptides, the length of single chain peptides, and the amount of overlap between single chain peptides will depend on several characteristics of the protein of interest, including the length. These factors can be determined by one skilled in the art without undue experimentation through the use of commercially available computer programs, such as Potean II™ (Proteus) and SPOT™. This allows for several possible epitopes to be encompassed within the OSPF of the present invention, therefore eliminating the cumbersome and expensive step of epitope identification.

In yet another embodiment, the protein of interest includes, but is not limited to, HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340);

anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230).); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235). For example, OSPFs for HIV-1 Gag include the peptides set forth as SEQ ID NO:1-122 and/or SEQ ID NO:236-335 and OSPFs for SIV Envelope protein include the peptides set forth as SEQ ID NO:123-206 and/or 336-338. For example, OSPFs for HIV-1 Gag include the peptides set forth as SEQ ID NO:1-122 and/or SEQ ID NO:236-335 and OSPFs for SIV Envelope protein include the peptides set forth as SEQ ID NO:123-206 and/or 336-338.

***Therapeutic Methods***

The present invention provides for therapeutic methods of treating subjects (*e.g.*, vertebrates, such as humans). In one aspect, the invention pertains to a method of treating an OSPF-associated disorder, *e.g.*, any disease, disorder, or condition which can be treated or prevented by modulating an immune response, *i.e.*, a Th1-mediated immune response such as a CTL-mediated immune response or a Th2-mediated immune response, such as an antibody-associated response, in a subject. In one embodiment, the present invention includes administering to a subject having an

OSPF-associated disorder, an effective amount of an OSPF of the present invention, thereby treating the OSPF-associated disorder in the subject.

Also within the scope of this invention is the administration of an OSPF prophylactically. Administration of an OSPF of the present invention can occur prior to the manifestation of symptoms of an OSPF-associated disorder, such that the disorder is prevented or, alternatively, delayed in its progression. The prophylactic methods of the present invention can be carried out in a similar manner to the therapeutic methods described herein, although dosage and treatment regimens may differ.

Accordingly, the present method has therapeutic utility in modulating an immune response. In one embodiment, the present method has therapeutic utility in biasing an immune response towards a Th1-mediated (*i.e.*, CTL-mediated) immune response depending upon the desired therapeutic regimen. In another embodiment, the present invention has therapeutic utility in biasing an immune response towards a Th2-mediated (*i.e.*, antibody-associated immunity). Such methods are particularly useful in diseases such as viral infections (*e.g.*, Ebola virus, hepatitis C, HIV, *e.g.*, HIV-1 and HIV-2, RSV, monkeypox, and SARS coronavirus), bacterial infections (*e.g.*, anthrax, Listeria monocytogenes, Legionella and mycobacterium such as tuberculosis), parasitic infections (*e.g.* malaria) protection against toxins (*e.g.*, shigella toxin, toxin botulinum and tetanus toxin), prion diseases, and neoplastic diseases (*e.g.*, breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal (*e.g.*, pancreatic and stomach) cancer and osteogenic sarcoma).

In another aspect, the invention provides a vaccine for immunizing a subject against an OSPF-associated disorder, wherein the vaccine comprises an OSPF of the present invention, either alone or dispersed in a physiologically acceptable, nontoxic vehicle in an amount is effective to immunize a subject against an OSPF disorder.

The vaccines of the present invention are administered in a manner compatible with the dosage formulation, and in such amount as will be therapeutically effective and immunogenic. The quantity to be administered depends on the subject to be treated, capacity of the subject's immune system to generate a cellular immune response, and degree of protection desired. Precise amounts of active ingredient required to be administered depend on the judgment of the practitioner and are

peculiar to each individual. However, suitable dosage ranges are of the order of about one microgram to about one milligram, preferably about 25 micrograms and more preferably about 30 micrograms active ingredient per kilogram per 70 kilogram individual. Suitable regimes for initial administration and booster shots are also variable, but are typified by an initial administration followed in one or two week intervals by a subsequent injection or other administration. Also within the scope of the invention is the co-administration of an adjuvant in combination with an OSPF of the present invention. Suitable adjuvants include, but are not limited to, IL-2, IL-12, IL-15, alum, Conconvalin A, phorbol esters and Freud's adjuvant.

In yet another aspect, the invention features a kit for immunizing a subject against an OSPF-associated disorder wherein the kit comprises an OSPF of the present invention and may further comprise instructions for use.

In yet another aspect, the invention features a vaccine adjuvant which comprises an OSPF of the present invention and a pharmaceutically acceptable carrier which may be used to enhance the efficacy of a vaccine.

***Pharmaceutical Compositions and Uses thereof***

Another aspect of the present invention provides pharmaceutically-acceptable compositions which comprise an OSPF and a pharmaceutically-acceptable carrier(s), in an amount effective to modulate a CTL-mediated immune response.

In a particular embodiment, the OSPF is administered to the subject using a pharmaceutically-acceptable formulation, *e.g.*, a pharmaceutically-acceptable formulation that provides sustained delivery of the OSPF to a subject for at least 12 hours, 24 hours, 36 hours, 48 hours, one week, two weeks, three weeks, or four weeks after the pharmaceutically-acceptable formulation is administered to the subject.

In certain embodiments, these pharmaceutical compositions are suitable for oral administration to a subject. In other embodiments, as described in detail below, the pharmaceutical compositions of the present invention may be specially formulated for administration in solid or liquid form, including those adapted for the following: (1) oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, boluses, powders, granules, pastes; (2) parenteral administration, for example, by subcutaneous, intramuscular or intravenous injection as, for example, a sterile solution or suspension; (3) topical application, for example,

as a cream, ointment or spray applied to the skin; (4) intravaginally or intrarectally, for example, as a pessary, cream or foam; or (5) aerosol, for example, as an aqueous aerosol, liposomal preparation or solid particles containing the compound.

As used herein, the term "effective amount" includes an amount effective, at dosages and for periods of time necessary, to achieve the desired result, *e.g.*, sufficient to modulate a CTL-mediated immune response. An effective amount of OSPF, as defined herein may vary according to factors such as the disease state, age, and weight of the subject, and the ability of the OSPF to elicit a desired response in the subject. Dosage regimens may be adjusted to provide the optimum therapeutic response. An effective amount is also one in which any toxic or detrimental effects (*e.g.*, side effects) of the OSPF of the present invention are outweighed by the therapeutically beneficial effects.

A therapeutically effective amount of OSPF (*i.e.*, an effective dosage) may range from about 0.001 to 40 μg/kg body weight, preferably about 0.01 to 30 μg/kg body weight per 70 kilogram individual. The skilled artisan will appreciate that certain factors may influence the dosage required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of an OSPF can include a single treatment or, can include a series of treatments. In one example, a subject is treated with an OSPF in the range of between about 0.1 to 30 μg/kg body weight, one time per week for between about 1 to 10 weeks, preferably between 2 to 8 weeks, more preferably between about 3 to 7 weeks, and even more preferably for about 4, 5, or 6 weeks. It will also be appreciated that the effective dosage of an OSPF used for treatment may increase or decrease over the course of a particular treatment.

The methods of the invention further include administering to a subject a therapeutically effective amount of an OSPF in combination with another pharmaceutically active compound known to modulate, for example, a CTL-mediated immune responses, *e.g.*, agents such as interleukins (IL) (*e.g.* IL-2, IL-12, IL-15), lipopolysaccharide (LPS), concanavalin A (ConA), phorbol esters, and ionomycin. Other pharmaceutically active compounds that may be used to modulate a TH2-mediated immune response, for example, can be found in *Harrison's Principles of*

*Internal Medicine*, Thirteenth Edition, Eds. T.R. Harrison *et al.* McGraw-Hill N.Y., NY; and the Physicians Desk Reference 50th Edition 1997, Oradell New Jersey, Medical Economics Co., the complete contents of which are expressly incorporated herein by reference. The OSPF and the pharmaceutically active compound may be administered to the subject in the same pharmaceutical composition or in different pharmaceutical compositions (at the same time or at different times).

The regimen of administration also can affect what constitutes an effective amount. OSPFs of the present invention can be administered to the subject prior to, simultaneously with, or after the administration of the other agent(s). Further, several divided dosages, as well as staggered dosages, can be administered daily or sequentially, or the dose can be proportionally increased or decreased as indicated by the exigencies of the therapeutic situation.

The phrase "pharmaceutically acceptable" is employed herein to refer to those OSPFs of the present invention, compositions containing such compounds, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

The phrase "pharmaceutically-acceptable carrier" as used herein means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material, involved in carrying or transporting the subject chemical from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the subject. Some examples of materials which can serve as pharmaceutically-acceptable carriers include: (1) sugars, such as lactose, glucose and sucrose; (2) starches, such as corn starch and potato starch; (3) cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; (4) powdered tragacanth; (5) malt; (6) gelatin; (7) talc; (8) excipients, such as cocoa butter and suppository waxes; (9) oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; (10) glycols, such as propylene glycol; (11) polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; (12) esters, such as ethyl oleate and ethyl laurate; (13) agar; (14) buffering agents, such as magnesium

hydroxide and aluminum hydroxide; (15) alginic acid; (16) pyrogen-free water; (17) isotonic saline; (18) Ringer's solution; (19) ethyl alcohol; (20) phosphate buffer solutions; and (21) other non-toxic compatible substances employed in pharmaceutical formulations.

Wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions.

Examples of pharmaceutically-acceptable antioxidants include: (1) water soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; (2) oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol, and the like; and (3) metal chelating agents, such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

Compositions containing an OSPF(s) include those suitable for oral, nasal, topical (including buccal and sublingual), rectal, vaginal, aerosol and/or parenteral administration. The compositions may conveniently be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, the particular mode of administration. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect. Generally, out of one hundred per cent, this amount will range from about 1 per cent to about ninety-nine percent of active ingredient, preferably from about 5 per cent to about 70 per cent, most preferably from about 10 per cent to about 30 per cent.

Methods of preparing these compositions include the step of bringing into association an OSPF(s) with the carrier and, optionally, one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association an OSPF with liquid carriers, or finely divided solid carriers, or both, and then, if necessary, shaping the product.

Compositions of the invention suitable for oral administration may be in the form of capsules, cachets, pills, tablets, lozenges (using a flavored basis, usually sucrose and acacia or tragacanth), powders, granules, or as a solution or a suspension in an aqueous or non-aqueous liquid, or as an oil-in-water or water-in-oil liquid emulsion, or as an elixir or syrup, or as pastilles (using an inert base, such as gelatin and glycerin, or sucrose and acacia) and/or as mouth washes and the like, each containing a predetermined amount of an OSPF(s) as an active ingredient. An OSPF may also be administered as a bolus, electuary or paste.

In solid dosage forms of the invention for oral administration (capsules, tablets, pills, dragees, powders, granules and the like), the active ingredient is mixed with one or more pharmaceutically-acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: (1) fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and/or silicic acid; (2) binders, such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; (3) humectants, such as glycerol; (4) disintegrating agents, such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; (5) solution retarding agents, such as paraffin; (6) absorption accelerators, such as quaternary ammonium compounds; (7) wetting agents, such as, for example, acetyl alcohol and glycerol monostearate; (8) absorbents, such as kaolin and bentonite clay; (9) lubricants, such a talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof; and (10) coloring agents. In the case of capsules, tablets and pills, the pharmaceutical compositions may also comprise buffering agents. Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like.

A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using binder (for example, gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Molded tablets may be made by molding in a suitable machine a mixture of the powdered active ingredient moistened with an inert liquid diluent.

The tablets, and other solid dosage forms of the pharmaceutical compositions of the present invention, such as dragees, capsules, pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethyl cellulose in varying proportions to provide the desired release profile, other polymer matrices, liposomes and/or microspheres. They may be sterilized by, for example, filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved in sterile water, or some other sterile injectable medium immediately before use. These compositions may also optionally contain opacifying agents and may be of a composition that they release the active ingredient(s) only, or preferentially, in a certain portion of the gastrointestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes. The active ingredient can also be in micro-encapsulated form, if appropriate, with one or more of the above-described excipients.

Liquid dosage forms for oral administration of the OSPF(s) include pharmaceutically-acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredient, the liquid dosage forms may contain inert diluents commonly used in the art, such as, for example, water or other solvents, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, coloring, perfuming and preservative agents.

Suspensions, in addition to the active OSPF(s) may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, and mixtures thereof.

Pharmaceutical compositions of the invention for rectal or vaginal administration may be presented as a suppository, which may be prepared by mixing one or more OSPF(s) with one or more suitable nonirritating excipients or carriers comprising, for example, cocoa butter, polyethylene glycol, a suppository wax or a salicylate, and which is solid at room temperature, but liquid at body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active agent.

Compositions of the present invention which are suitable for vaginal administration also include pessaries, tampons, creams, gels, pastes, foams or spray formulations containing such carriers as are known in the art to be appropriate.

Dosage forms for the topical or transdermal administration of an OSPF(s) include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. The active OSPF(s) may be mixed under sterile conditions with a pharmaceutically-acceptable carrier, and with any preservatives, buffers, or propellants which may be required.

The ointments, pastes, creams and gels may contain, in addition to OSPF(s) of the present invention, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

Powders and sprays can contain, in addition to an OSPF(s), excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates and polyamide powder, or mixtures of these substances. Sprays can additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

The OSPF(s) can be alternatively administered by aerosol. This is accomplished by preparing an aqueous aerosol, liposomal preparation or solid particles containing the compound. A nonaqueous (*e.g.*, fluorocarbon propellant) suspension could be used. Sonic nebulizers are preferred because they minimize exposing the agent to shear, which can result in degradation of the compound.

Ordinarily, an aqueous aerosol is made by formulating an aqueous solution or suspension of the agent together with conventional pharmaceutically-acceptable carriers and stabilizers. The carriers and stabilizers vary with the requirements of the particular compound, but typically include nonionic surfactants (Tweens, Pluronics, or polyethylene glycol), innocuous proteins like serum albumin, sorbitan esters, oleic

acid, lecithin, amino acids such as glycine, buffers, salts, sugars or sugar alcohols. Aerosols generally are prepared from isotonic solutions.

Transdermal patches have the added advantage of providing controlled delivery of an OSPF(s) to the body. Such dosage forms can be made by dissolving or dispersing the agent in the proper medium. Absorption enhancers can also be used to increase the flux of the active ingredient across the skin. The rate of such flux can be controlled by either providing a rate controlling membrane or dispersing the active ingredient in a polymer matrix or gel.

Ophthalmic formulations, eye ointments, powders, solutions and the like, are also contemplated as being within the scope of this invention.

Pharmaceutical compositions of this invention suitable for parenteral administration comprise one or more OSPF(s) in combination with one or more pharmaceutically-acceptable sterile isotonic aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions just prior to use, which may contain antioxidants, buffers, bacteriostats, solutes which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents.

Examples of suitable aqueous and nonaqueous carriers which may be employed in the pharmaceutical compositions of the invention include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents, such as sugars, sodium chloride, and the like into the compositions. In addition, prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents which delay absorption such as aluminum monostearate and gelatin.

In some cases, in order to prolong the effect of a drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material having poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally-administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

Injectable depot forms are made by forming microencapsule matrices of OSPF(s) in biodegradable polymers such as polylactide-polyglycolide. Depending on the ratio of drug to polymer, and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions which are compatible with body tissue.

When the OSPF(s) are administered as pharmaceuticals, to humans and animals, they can be given per se or as a pharmaceutical composition containing, for example, 0.1 to 99.5% (more preferably, 0.5 to 90%) of active ingredient in combination with a pharmaceutically-acceptable carrier.

The term "administration" or "administering" is intended to include routes of introducing the OSPF(s) to a subject to perform their intended function. Examples of routes of administration which can be used include injection (subcutaneous, intravenous, parenterally, intraperitoneally, intrathecal), oral, inhalation, rectal and transdermal. The pharmaceutical preparations are, of course, given by forms suitable for each administration route. For example, these preparations are administered in tablets or capsule form, by injection, inhalation, eye lotion, ointment, suppository, etc. administration by injection, infusion or inhalation; topical by lotion or ointment; and rectal by suppositories. Oral administration is preferred. The injection can be bolus or can be continuous infusion. Depending on the route of administration, the OSPF can be coated with or disposed in a selected material to protect it from natural conditions which may detrimentally effecting its ability to perform its intended function. The OSPF can be administered alone, or in conjunction with either another agent as described above or with a pharmaceutically-acceptable carrier, or both. The OSPF can be administered prior to the administration of the other agent,

simultaneously with the agent, or after the administration of the agent. Furthermore, the OSPF can also be administered in a proform which is converted into its active metabolite, or more active metabolite *in vivo*.

The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticulare, subcapsular, subarachnoid, intraspinal and intrasternal injection and infusion.

The phrases "systemic administration," "administered systemically", "peripheral administration" and "administered peripherally" as used herein mean the administration of an OSPF(s), drug or other material, such that it enters the subject's system and, thus, is subject to metabolism and other like processes, for example, subcutaneous administration.

Regardless of the route of administration selected, the OSPF(s), which may be used in a suitable hydrated form, and/or the pharmaceutical compositions of the present invention, are formulated into pharmaceutically-acceptable dosage forms by conventional methods known to those of skill in the art.

***Examples***

The invention is further illustrated by the following examples which in no way should be construed as being further limiting.

## 1. Example 1: HIV and SIV

*Materials and Methods*

A. Peptides

OSPFs corresponding to HIV Gag (SEQ ID NOs:1-122) represent a group of peptides of 15 amino acids in length, with 11-amino acid overlaps between sequential peptides, and spanning the entire HIV Gag protein. Most peptides were approximately 80% pure. OSPFs corresponding to SIV Env (SEQ ID NOs:123-206 and/or 336-338), represent a group of peptides of 20 amino acids in length, with 10 amino acid overlaps between sequential peptides, and spanning the entire SIV Env protein. Most peptides are approximately 80% pure.

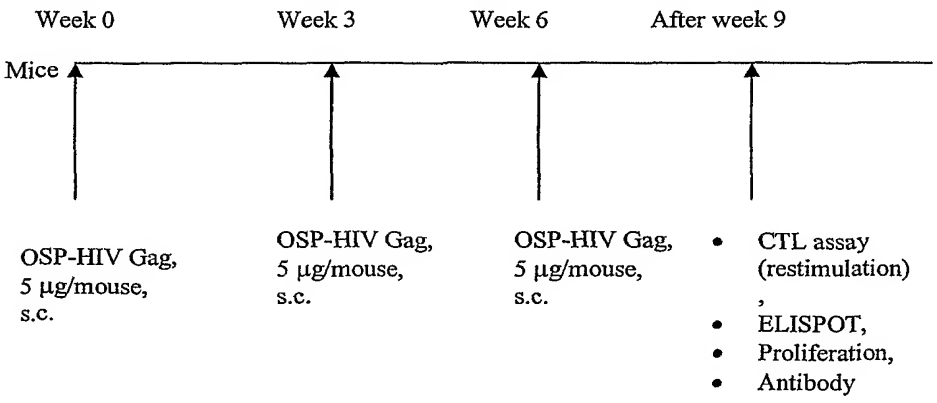
Peptide P7G (AMQMLKETI (SEQ ID NO:207)) is an H-2K$^d$-restricted CTL epitope of HIV p24 antigen (see, *e.g.*, Doe, B and Walker, C. (1996) *AIDS* 10:793). This peptide was made by the Molecular Biology Core Facilities at the Dana-Farber Cancer Institute (DFCI), and was used as a positive control. The peptide was greater than approximately 97% pure.

A non-epitope peptide, HIV clade C envelope V3 peptide (GPGQAFYAT (SEQ ID NO:208) made by the Molecular Biology Core Facilities, at Dana Farber Cancer Institute, Boston, MA, was used as a negative control peptide. The peptide was approximately 97% pure.

**B.** Mice and Immunization

BALB/c (H-2$^d$) and C57BL/6 (H-2$^b$) (Taconic Farms, NY), were immunized subcutaneously (s.c.) with OSPF-HIV Gag. Each mouse was immunized with 5 μg of each peptide, combined with MLP + TDM Adjuvant System (Sigma, St. Louis, MO; product number M6536. Peptides were >80% pure.). The HIV Gag OSPF was a series of peptides, each 15 amino acids in length, with 11-amino acid overlaps between sequential peptide (NIH AIDS Research and Reference Reagent Program Catalog #5107). Control mice were given adjuvant alone (mock immunization). The immunization regimen is shown below in Table 1:

**Table 1:**



C. Blood Donors and Isolation and Differentiation of Blood Dendritic Cells

Leukopacks were provided by anonymous, normal blood donors (Dana-Farber Cancer Institute Blood Bank, Boston, MA). These donors were MHC tissue-typed in Brigham and Women's Hospital (Boston, MA) and shown to have different MHC antigens. Dendritic cells (DC) were isolated and differentiated from peripheral blood mononuclear cells (PBMC). PBMC were cultured in plastic cell-culture flasks and incubated for 2 hrs at 5% $CO_2$ and 37°C. The adherent cells were collected and incubated in complete RPMI supplemented with interleukin–4 (IL-4) and granulocyte-macrophage colony stimulating factor (GM-CSF) (Stem Cell Technology, Vancouver, Canada) (DC medium). An additional 2 ml of DC medium was added to the culture each day. On day 6, detached cells were collected and transferred into a new flask with fresh DC medium. The purity of the DC cell population was assessed using monoclonal antibodies against specific DC markers (see, *e.g.*, Popov, S., unpublished data). These DC were pulsed overnight with OSPF-SIV Env. The OSPF-SIV Env are a series of peptides of 20 amino acids in length, with 10-amino acid overlaps between sequential peptides (NIH AIDS Research and Reference Reagent Program Catalog #4625). Peptides were >80% pure. DC were irradiated and used to generate CTL in vitro by 3 stimulation of autologous PBMC at weekly interval. A CTL assay or ELISPOT was performed one week after the last stimulation.

D. Cytotoxic T Lymphocyte (CTL) Assays

Murine CTL Assays:

For the mouse CTL assay, effector cells were splenic mononuclear cells which were isolated from OSPF- or adjuvant-only immunized mice and restimulated (2 x $10^6$/ml) *in vitro* with 1 μM peptide for 7-10 days. Target cells were P815 cells (H-$2^d$, for BALB/c mice) and EL-4 cells (H-$2^b$, for B57BL/6 mice). Target cells were labeled with $^{51}Cr$ (70 μCi/2 x $10^6$ cells; Perkin-Elmer, Boston, MA) and pulsed overnight with or without OSPF-HIV Gag (1 μM), or infected overnight with vaccinia virus [2 plaque forming unit (pfu)/target cell] expressing HIVgag (NIH AIDS Research and Reference Reagent Program cat # vP1289), or wild type vaccinia virus (Therion, Cambridge, MA).

In the case of H-$2^d$ restricted CTL, a known CTL epitope from HIV p24 antigen P7G (AMQMLKETI)[19] (SEQ ID NO:207) (> 97% pure, Molecular Biology Core Facilities, Dana farer Cancer Institute, Boston, MA) was included to test if OSPF-HIV Gag could generate P7G specific (H-$2^d$ restricted) CTL in BALB/c mice. A non-epitopic peptide, HIV clade C envelope V3 peptide (GPGQAFYAT) (SEQ ID NO:208), (> 97% pure, Molecular Biology Core Facilities, Dana Farber Cancer Institute, Boston, MA), was used as negative control peptide.

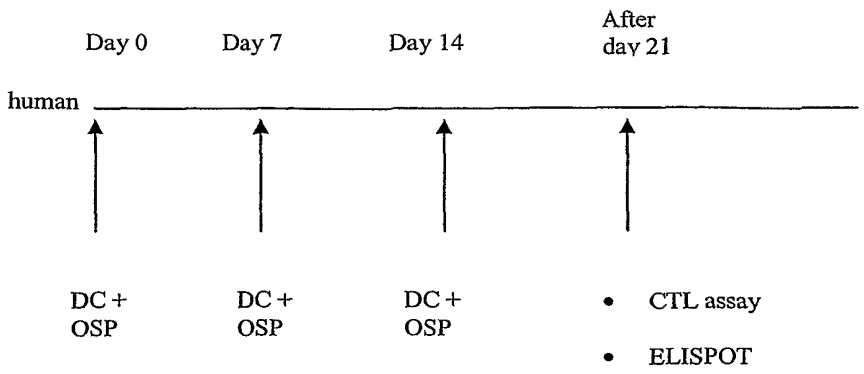
Effector cells and target cells were co-cultured at different ratios for 6 h, and cytolysis was determined by $^{51}$Cr release from target cells (see, *e.g.*, Wunderlich *et al.*, (1997) Current Protocols in Immunology 3.11.1-3.11.20). The percentage specific $^{51}$Cr release was calculated as: 100 (experimental release – spontaneous release)/ (maximum release – spontaneous release). Maximum release was determined from supernatants of cells that were lysed by addition of 5% Triton-X 100. Spontaneous release was determined from the target cells incubated without addition of effector cells.

Human CTL Assays:

For the human CTL assay, effector cells were PBMC stimulated with irradiated autologous DC that had been pulsed with or without OSPF cells (see Table 2).Target cells were EBV-transformed, autologous B cell lines. These cells were labeled with $^{51}$Cr (70 μCi/2 x $10^6$ cells; Perkin-Elmer, Boston, MA) and pulsed overnight with or without OSPF-SIV Env (1 μM), or infected overnight with vaccinia virus [2 plaque forming unit (pfu)/target cell] expressing SIV gag-pol-env, or wild type vaccinia virus (Vaccinia virus expressing SIV gag-pol-env and wild type vaccinia virus were obtained from Therion, Cambridge, MA).

Effector cells and target cells were co-cultured and the percentage specific $^{51}$Cr release was calculated as described above in the mouse CTL assay section (see, *e.g.*, Wunderlich, *et al.*, *supra*).

**Table 2:**




E. ELISPOT™ Assay

Human and mouse ELISPOT assays were performed using ELISPOT kits from BioSource International (Camarillo, CA). Briefly, following the final stimulation, mouse splenocytes or human PBMC stimulated with DC (treated with OSPF and untreated) were seeded into anti-interferon gamma (anti-IFN-γ ) monoclonal antibody coated 96-well plates and incubated overnight at 4°C. Subsequently, the cells were discarded and biotinated- anti-IFN-γ antibodies were added for an hour at 37°C followed by another hour of incubation at 37°C with anti-biotin antibody labeled with enzyme. After the color reaction developed, spots were counted under a microscope. Results were expressed as spot forming units (SFU)/$10^6$ cells.

F. Lymphocyte Proliferation Assay

Splenic lymphocytes were isolated and cultured at 2 x $10^6$ / ml in RPMI 1640 plus 15 % FCS and antibiotics in the presence of HIV Gag protein (15 ug/ml), OSPF-HIV Gag (3 ug/ml) or ovalbumin (OVA) (15 ug/ml) for 5 days. Four hours prior to harvesting, cells were pulsed with 1 uCI per well of $^3$H-thymidine. After cells were harvested, $^3$H-thymidine incorporation was assessed using a β-counter (Beckman). Results were expressed as count per minute (cpm).

*Results*

A. OSPF-HIV Gag can promiscuously induce CTL responses in genetically different mice

To determine whether OSPF were able to induce CTL responses in genetically different mice, BALB/c (H-$2^d$) and C57BL/6 (H-$2^b$) mice were immunized subcutaneously three times at three-week intervals with OSPF-HIV Gag together with an oil-in-water adjuvant system MPL+TDM. CTL activity in both mouse strains against OSPF-HIV Gag was detected by $^{51}$Cr release assays (Figure 1a). No CTL activity was detected in the control mice (adjuvant only). Moreover, these CTLs were also capable of killing target cells infected with vaccinia virus engineered to express HIV Gag (Figure 1b), and, in the case of BALB/c mice, and HIV Gag specific, H-2K$^d$ restricted epitope P7G (Figure 1c). These results suggest that not only are OSPF-HIV Gag able to generate specific CTLs, but these cells are capable of killing cells which express HIV-Gag protein.

B. OSPF-HIV Gag can induce proliferative Th cell responses in genetically different mice

To determine whether OSPF are capable of stimulating a proliferative Th cell response, BALB/c and C57BL/6 were immunized with OSPF-HIV Gag as described above. Splenocytes were recovered and cultured *in vitro* with either soluble HIV Gag protein, OSPF-HIV Gag or ovalbumin as a control. The proliferative response was measured by the percentage of $^3$H-thymidine incorporation (Figure 2). These results demonstrate that OSPF can induce a proliferative Th response and that immunizing with OSPF provides the same proliferative Th-mediated response as does that of the intact protein.

C. *Ex vivo* Induction of Dendritic Cells and Autologous PBMCs of Human Individuals with Different MHC Class I Backgrounds

OSPF that corresponded to SIV Env (OSPF-SIV Env) were used to induce the virus-specific CTL responses *ex vivo* using cells from human blood leukopacks (dendritic cells (DC) and autologous PBMC). OSPF-SIV Env are a group of 87 peptides of 20 amino acids in length, with 10 amino acid overlaps between sequential

peptides, and spanning the entire SIV Env protein OSP promiscuously induced CTL in different individuals of different MHC backgrounds.

Cells from two human blood leukopacks from two anonymous donors (d#1 and d#2) were collected and their MHC class I (HLA – A, B, C) were tested [d#1: HLA-A (02, blank); B (08, 18); Bw4 (-,-); Bw6 (+,+); Cw(07, blank). D#2: HLA-A (11, 24); B (39, 51); Bw4 (-,+); Bw6 (+,-); Cw (07, 14). The peripheral blood monocytes (PBMC) were separated and stimulated three times in vitro with irradiated autologous dendritic cells (DC) pulsed with or without OSPF-SIV Env at weekly intervals and ELISPOT and chromium release assays were performed one week after the last stimulation.

These results show that PBMC stimulated with DC pulsed with OSPF-SIV Env generated interferon-γ secreted cells in both d#1 and d#2 (Figure 3a). The chromium release assay showed that target cells transfected with vaccinia virus expressing SIV gag-pol-env were also killed by CTL (Figure 3b). There was no killing when effector and target cells from two leukopacks were mismatched (data not shown), indicating that the APC from the two leukopacks did not present the same epitopes and the killing was MHC restricted.

*Conclusions*

These results show that an individual OSPF can generate CTL activity and proliferative Th cell mediated responses in genetically different strains of mice. Furthermore, OSPF can generate CTL activity in human cells with different HLA subtypes. The data also shows that immunization with OSPF(s) can result in the generation of antigen-specific CTL cells capable of lysing virally-infected cells (*i.e.* cells pulsed with OSPF, target cells infected with vaccinia expressing HIV genes and target cells pulsed with virus-specific epitopic peptide P7G (AMQMLKETI) (SEQ ID NO:207). Thus, since OSPF(s) are capable of generating a Th proliferative response and CTLs in genetically diverse individuals/animals, there is no need to identify specific CTL epitopes.

## 2. Example 2: RSV

### A. Materials and Methods

Potential OSPFs corresponding to RSV fusion protein (SEQ ID NO:214) are shown as follows (The numbered and underlined sequences represent the single chain peptide sequences):

MELLILKANA ITTILTAVTF CFASGQNITE EFYQSTCSAV SKGYLSALRT
1 2 3
GWYTSVITIE LSNIKENKCN GTDAKVKLIK QELDKYKNAV TELQLLMQST
4 5 6 7 8
PPTNNRARRE LPRFMNYTLN NAKKTNVTLS KKRKRRFLGF LLGVGSAIAS
9 10 11 12 13
GVAVSKVLHL EGEVNKIKSA LLSTNKAVVS LSNGVSVLTS KVLDLKNYID
14 15 16 17 18
KQLLPIVNKQ SCSISNIETV IEFQQKNNRL LEITREFSVN AGVTTPVSTY
19 20 21 22 23
MLTNSELLSL INDMPITNDQ KKLMSNNVQI VRQQSYSIM SIIKEEVLAYV
24 25 26 27 28
VQLPLYGVI DTPCWKLHTSP LCTTNTKEGS NICLTRTDRG WYCDNAGSVS
29 30 31 32 33
FFPQAETCKV QSNRVFCDTM NSLTLPSEIN LCNVDIFNPK YDCKIMTSKT
34 35 36 37 38
DVSSSVITSL GAIVSCYGKT KCTASNKNRG IIKTFSNGCD YVSNKGMDTV
39 40 41 42 43
SVGNTLYYVN KQEGKSLYVK GEPIINFYDP LVFPSDEFDA SISQVNEKIN
44 45 46 47 48
QSLAFIRKSD ELLHNVNAGK STTNIMITTI IIVIIVILLS LIAVGLLLYC
49 50 51 52 53
KARSTPVTLS KDQLSGINNI AFSN
54 55 (13mer)

The OSPFs corresponding to the RSV fusion protein represent a group of 55 peptides of 15 amino acids in length, with 5 amino acid overlaps between sequential peptides, and spanning the entire RSV fusion protein.

Examples of other proteins of interest which can be used in the present invention, include, but are not limited to, anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2

envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

B. Vaccinia Viruses

Vaccinia viruses expressing RSV fusion protein may be utilized and can be made using routine techniques known to those skilled in the art to conduct CTL assays *in vitro*.

C. Mice and Immunization

BALB/c (H-$2^d$) and C57BL/6 (H-$2^b$) are immunized subcutaneously (s.c.) with OSPF of RSV fusion protein at 5 μg of each individual peptide per mouse together with MLP + TDM Adjuvant system (Sigma, St. Louis, MO; product number M6536. Peptides were >80% pure). Control mice are given only the adjuvant (mock immunization) according to the regimen described in Example 1.

D. Blood Donors and Isolation and Differentiation of Blood Dendritic Cells

Leukopacks may be provided by anonymous, normal blood donors. These donors are MHC tissue-typed and dendritic cells isolated and differentiated as previously described above in Example 1.

E. Cytotoxic T Lymphocyte (CTL) Assays

Murine CTL Assays:

For the mouse CTL assay, effector cells are splenic mononuclear cells which are isolated from OSPF- or adjuvant-only immunized mice and restimulated (2 x $10^6$/ml) in vitro with 1 μM peptide for 7-10 days. Target cells are P815 cells (H-$2^d$, for BALB/c mice) and EL-4 cells (H-$2^b$, for B57BL/6 mice). Target cells are labeled with $^{51}$Cr (70 μCi/2 x $10^6$ cells; Perkin-Elmer, Boston, MA) and pulsed overnight with or without OSPF-RSV fusion protein (1 μM), or infected overnight with vaccinia virus [2 plaque forming unit (pfu)/target cell].

Effector cells and target cells are co-cultured at different ratios for 6 h, and cytolysis is determined by $^{51}$Cr release from target cells (see, *e.g.*, Wunderlich *et al.*, (1997) Current Protocols in Immunology 3.11.1-3.11.20). The percentage specific $^{51}$Cr release is calculated as: 100 (experimental release – spontaneous release)/ (maximum release – spontaneous release). Maximum release is determined from supernatants of cells that are lysed by addition of 5% Triton-X 100. Spontaneous release is determined from the target cells incubated without addition of effector cells.

Human CTL Assays:

For the human CTL assay, effector cells are PBMC stimulated with irradiated autologous DC that are pulsed with or without OSPF (see Table 2).Target cells are EBV-transformed, autologous B cell lines. These cells are labeled with $^{51}$Cr (70 μCi/2 x $10^6$ cells; Perkin-Elmer, Boston, MA) and pulsed overnight with or without OSPF RSV fusion protein (1 μM), or infected overnight with vaccinia virus [2 plaque forming unit (pfu)/target cell] expressing SIV gag-pol-env, or wild type vaccinia virus (Vaccinia virus expressing SIV gag-pol-env and wild type vaccinia virus are obtained from Therion, Cambridge, MA).

Effector cells and target cells are co cultured and the percentage specific $^{51}$Cr release is calculated as described above in the mouse CTL assay section (see, *e.g.*, Wunderlich, *et al.*, *supra*).

F. ELISPOT™ Assay

Human and mouse ELISPOT assays are performed using ELISPOT kits from BioSource International (Camarillo, CA). Briefly, following the final stimulation,

mouse splenocytes or human PBMC are stimulated with DC (treated with OSPF and untreated) and seeded into anti-interferon gamma (anti-IFN-γ ) monoclonal antibody coated 96-well plates and incubated overnight at 4°C. Subsequently, the cells are discarded and biotinated- anti-IFN-γ antibodies are added for an hour at 37°C followed by another hour of incubation at 37°C with anti-biotin antibody labeled with enzyme. After the color reaction develops, spots are counted under a microscope. Results are expressed as spot forming units (SFU)/$10^6$ cells.

G. Lymphocyte Proliferation Assay

Splenic lymphocytes are isolated and cultured at 2 x $10^6$ / ml in RPMI 1640 plus 15 % FCS plus antibiotics in the presence of RSV fusion protein (15 ug/ml) or OSPF-RSV fusion protein or ovalbumin (OVA) for 5 days. Four hours before harvesting, cells are pulsed with 1 uCI per well of $^3$H-thymidine. After cells are harvested, $^3$H-thymidine incorporation is assessed using a β-counter (Beckman). Results are expressed as count per minute (cpm).

**Incorporation by Reference**

The contents of all references (including literature references, issued patents, published patent applications, and co-pending patent applications) cited throughout this application are hereby expressly incorporated herein in their entireties by reference.

**Equivalents**

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents of the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

## CLAIMS

1. A method of modulating an immune response comprising administering to a subject an effective amount of an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein at least one single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said immune response is modulated.

2. The method of claim 1, wherein said subject is a vertebrate.

3. The method of claim 1, wherein said Y is fifteen (15) amino acids.

4. The method of claim 1, wherein said Z is five (5) amino acids.

5. The method of claim 1, wherein said immune response is a Th1-mediated immune response.

6. The method of claim 5, wherein said Th1-mediated immune response is a CTL-mediated immune response.

7. The method of claim 1, wherein said immune response is a Th2-mediated immune response.

8. The method of claim 7, wherein said Th2-mediated immune response is an antibody-associated immune response.

9. The method of claim 1, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

10. The method of claim 9, wherein said MHC Class I-bearing cell is a CTL.

11. The method of claim 1, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

12. The method of claim 11, wherein said MHC Class II-bearing cell is a B cell.

13. The method of claim 1, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

14. A method of modulating an immune response comprising administering to a subject an effective amount of an overlapping synthetic peptide formulation (OSPF),

wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said immune response is modulated.

15. The method of claim 14, wherein said subject is a vertebrate.

16. The method of claim 14, wherein said Y is fifteen (15) amino acids.

17. The method of claim 14, wherein said immune response is a Th1-mediated immune response.

18. The method of claim 17, wherein said Th1-mediated immune response is a CTL-mediated immune response.

19. The method of claim 14, wherein said immune response is a Th2-mediated immune response.

20. The method of claim 19, wherein said Th2-mediated immune response is an antibody-associated immune response.

21. The method of claim 13, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

22. The method of claim 21, wherein said MHC Class I-bearing cell is a CTL.

23. The method of claim 14, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

24. The method of claim 23, wherein said MHC Class II-bearing cell is a B cell.

25. The method of claim 14, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

26. A pharmaceutical composition comprising an overlapping synthetic peptide formulation (OSPF) and a pharmaceutically acceptable carrier, wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein at least one single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible.

27. The pharmaceutical composition of claim 26, wherein said Y is fifteen (15) amino acids.

28. The pharmaceutical composition of claim 27, wherein said Z is five (5) amino acids.

29. The pharmaceutical composition of claim 26, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

30. The pharmaceutical composition of claim 29, wherein said MHC Class I-bearing cell is a CTL.

31. The pharmaceutical composition of claim 26, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

32. The pharmaceutical composition of claim 31, wherein said MHC Class II-bearing cell is a B cell.

33. The pharmaceutical composition of claim 26, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile

enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

34. A pharmaceutical composition comprising an overlapping synthetic peptide formulation (OSPF) and a pharmaceutically acceptable carrier, wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides is such that internalization of said single chain peptide by a MHC -bearing cell and presentation by a MHC molecule to a T cell is possible.

35. The pharmaceutical composition of claim 13, wherein said Y is fifteen (15) amino acids.

36. The pharmaceutical composition of claim 34, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

37. The pharmaceutical composition of claim 36, wherein said MHC Class I-bearing cell is a CTL.

38. The pharmaceutical composition of claim 34, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

39. The pharmaceutical composition of claim 38, wherein said MHC Class II-bearing cell is a B cell.

40. The pharmaceutical composition of claim 34, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

41. A method of treating an OSPF-associated disorder in a subject comprising administering to a subject an effective amount of an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, and wherein at least one single chain peptide overlaps with another single chain peptide by a length of Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is treated in said subject.

42. The method of claim 41, wherein said subject is a vertebrate.

43. The method of claim 41, wherein said Y is fifteen (15) amino acids.

44. The method of claim 41, wherein said Z is five (5) amino acids.

45. The method of claim 41, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

46. The method of claim 45, wherein said MHC Class I-bearing cell is a CTL.

47. The method of claim 45, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

48. The method of claim 47, wherein said MHC Class II-bearing cell is a B cell.

49. The method of claim 41, wherein said protein of interest is selected from the group consisting of HIV Gag protein HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229);

pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

50. The method of claim 41, wherein said OSPF-associated disorder is a viral infection due to a virus.

51. The method of claim 50, wherein said virus is selected from the group consisting of HIV, *e.g.*, HIV-1 and HIV-2, human herpes viruses, cytomegalovirus ((esp. Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, Ebola virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18 and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus.

52. The method of claim 51, wherein said virus is Ebola virus.

53. The method of claim 49, wherein said protein of interest is Ebola virus nucleoprotein (SEQ ID NO:210).

54. The method of claim 41, wherein said OSPF-associated disorder is a bacterial infection due to a bacteria.

55. The method of claim 54, wherein said bacteria is selected from the group consisting of N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H. influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis;

Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S. typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii; Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae.

56. The method of claim 55, wherein said bacteria is B. anthracis.

57. The method of claim 49, wherein said protein of interest is anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209).

58. The method of claim 41, wherein said OSPF-associated disorder is a neoplastic disease.

59. The method of claim 58, wherein said neoplastic disease is selected from the group consisting of breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal cancer and osteogenic sarcoma.

60. The method of claim 59, wherein said neoplastic disease is melanoma.

61. The method of claim 49, wherein said protein of interest is melanoma antigen p15 (SEQ ID NO:212).

62. The method of claim 41, wherein said OSPF-associated disorder is a state of toxicity due to a toxin.

63. The method of claim 62, wherein said toxin is selected from the group consisting of botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin, aconotoxin, snake venom, scorpion venom and spider venoms.

64. The method of claim 62, wherein said toxin is pertussis.

65. The method of claim 49, wherein said protein of interest is pertussis toxin subunit 3 (SEQ ID NO:230).

66. The method of claim 41, wherein said OSPF-associated disorder is a parasitic infection due to a parasite.

67. The method of claim 66, wherein said parasite is selected from the group consisting of Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptosondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse, Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris.

68. The method of claim 67, wherein said parasite is Plasmodium.

69. The method of claim 49, wherein said protein of interest is circumsporozoite protein II (SEQ ID NO:224).

70. A method of treating an OSPF-associated disorder in a subject comprising administering to a subject an effective amount of an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides is such that internalization of said single chain peptide by a MHC -bearing cell and presentation by a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is treated in said subject.

71. The method of claim 70, wherein said subject is a vertebrate.

72. The method of claim 70, wherein said Y is fifteen (15) amino acids.

73. The method of claim 70, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

74. The method of claim 73, wherein said MHC Class I-bearing cell is a CTL.

75. The method of claim 70, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

76. The method of claim 75, wherein said MHC Class II-bearing cell is a B cell.

77. The method of claim 70, wherein said protein of interest is selected from the group consisting of HIV Gag (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG

protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

78. The method of claim 70, wherein said OSPF-associated disorder is a viral infection due to a virus.

79. The method of claim 78, wherein said virus is selected from the group consisting of HIV, *e.g.*, HIV-1 and HIV-2, human herpes viruses, cytomegalovirus (esp. Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, Ebola virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18 and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus.

80. The method of claim 79, wherein said virus is Ebola virus.

81. The method of claim 77, wherein said protein of interest is Ebola virus nucleoprotein (SEQ ID NO:210).

82. The method of claim 70, wherein said OSPF-associated disorder is a bacterial infection due to a bacteria.

83. The method of claim 82, wherein said bacteria is selected from the group consisting of N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H. influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis; Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S. typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii; Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae.

84. The method of claim 83, wherein said bacteria is B. anthracis.

85. The method of claim 77, wherein said protein of interest is anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209).

86. The method of claim 70, wherein said OSPF-associated disorder is a neoplastic disease.

87. The method of claim 86, wherein said neoplastic disease is selected from the group consisting of breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal cancer and osteogenic sarcoma.

88. The method of claim 87, wherein said neoplastic disease is melanoma.

89. The method of claim 77, wherein said protein of interest melanoma antigen p15 (SEQ ID NO:212).

90. The method of claim 70, wherein said OSPF-associated disorder is a state of toxicity due to a toxin.

91. The method of claim 90, wherein said toxin is selected from the group consisting of botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin, aconotoxin, snake venom, scorpion venom and spider venoms.

92. The method of claim 91, wherein said toxin is pertussis.

93. The method of claim 77, wherein said protein of interest is pertussis toxin subunit 3 (SEQ ID NO:230).

94. The method of claim 70, wherein said OSPF-associated disorder is a parasitic infection due to a parasite.

95. The method of claim 94, wherein said parasite is selected from the group consisting of Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptospondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse,

Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris.

96. The method of claim 95, wherein said parasite is Plasmodium.

97. The method of claim 77, wherein said protein of interest is circumsporozoite protein II (SEQ ID NO:224).

98. A vaccine for immunizing a subject against an OSPF-associated disorder by modulating a CTL-mediated immune response comprising a pharmaceutically acceptable carrier and an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptide is a length represented by Y, wherein Y at least 7 to (X-1) and X is the number of amino acids of said protein of interest, and wherein at least one single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible.

99. The vaccine of claim 98, wherein said subject is a vertebrate.

100. The vaccine of claim 98, wherein said Y is fifteen (15) amino acids.

101. The vaccine of claim 98, wherein said Z is five (5) amino acids.

102. The vaccine of claim 98, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

103. The vaccine of claim 102, wherein said MHC Class I-bearing cell is a CTL.

104. The vaccine of claim 98, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

105. The vaccine of claim 104, wherein said MHC Class II-bearing cell is a B cell.

106. The vaccine of claim 98, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

107. The vaccine of claim 98, wherein said OSPF-associated disorder is a viral infection due to a virus.

108. The vaccine of claim 107, wherein said virus is selected from the group consisting of HIV, *e.g.*, HIV-1 AND HIV-2, human herpes viruses, cytomegalovirus (esp. Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, Ebola virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18

and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus..

109. The vaccine of claim 108, wherein said virus is Ebola virus.

110. The vaccine of claim 105, wherein said protein of interest is Ebola virus nucleoprotein (SEQ ID NO:210).

111. The vaccine of claim 98, wherein said OSPF-associated disorder is a bacterial infection due to a bacteria.

112. The vaccine of claim 111, wherein said bacteria is selected from the group consisting of N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H. influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis; Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S. typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii; Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae.

113. The vaccine of claim 112, wherein said bacteria is B. anthracis.

114. The vaccine of claim 105, wherein said protein of interest is anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209).

115. The vaccine of claim 98, wherein said OSPF-associated disorder is a neoplastic disease.

116. The vaccine of claim 115, wherein said neoplastic disease is selected from the group consisting of breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal cancer and osteogenic sarcoma.

117. The vaccine of claim 116, wherein said neoplastic disease is melanoma.

118. The vaccine of claim 117, wherein said protein of interest is melanoma antigen p15 (SEQ ID NO:212).

119. The vaccine of claim 98, wherein said OSPF-associated disorder is a state of toxicity due to a toxin.

120. The vaccine of claim 119, wherein said toxin is selected from the group consisting of botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin, aconotoxin, snake venom, scorpion venom and spider venoms.

121. The vaccine of claim 120, wherein said toxin is pertussis.

122. The vaccine of claim 106, wherein said protein of interest is pertussis toxin subunit 3 (SEQ ID NO:230).

123. The method of claim 98, wherein said OSPF-associated disorder is a parasitic infection due to a parasite.

124. The method of claim 123, wherein said parasite is selected from the group consisting of Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptospondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse, Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris..

125. The method of claim 124, wherein said parasite is Plasmodium.

126. The method of claim 106, wherein said protein of interest is circumsporozoite protein II (SEQ ID NO:224).

127. A vaccine for immunizing a subject against an OSPF-associated disorder comprising a pharmaceutically acceptable carrier and an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides is such that internalization of said single chain peptide by a MHC -bearing cell and presentation by a MHC molecule to a T cell is possible.

128. The vaccine of claim 127, wherein said subject is a vertebrate.

129. The vaccine of claim 127, wherein said Y is fifteen (15) amino acids.

130. The vaccine of claim 127, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

131. The vaccine of claim 130, wherein said MHC Class I-bearing cell is a CTL.

132. The vaccine of claim 127, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

133. The vaccine of claim 132, wherein said MHC Class II-bearing cell is a B cell.

134. The vaccine of claim 127, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

135. The vaccine of claim 127, wherein said OSPF-associated disorder is a viral infection due to a virus.

136. The vaccine of claim 135, wherein said virus is selected from the group consisting of , HIV, *e.g.*, HIV-1 and HIV-2, human herpes viruses, cytomegalovirus

(esp. Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, Ebola virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18 and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus..

137. The vaccine of claim 136, wherein said virus is Ebola virus.

138. The vaccine of claim 134, wherein said protein of interest is Ebola virus nucleoprotein (SEQ ID NO:210).

139. The vaccine of claim 127, wherein said OSPF-associated disorder is a bacterial infection due toa bacteria.

140. The vaccine of claim 139, wherein said bacteria is selected from the group consisting of N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H. influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis; Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S. typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii;

Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae.

141. The vaccine of claim 140, wherein said bacteria is B. anthracis.

142. The vaccine of claim 134, wherein said protein of interest is anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209).

143. The vaccine of claim 127, wherein said OSPF-associated disorder is a neoplastic disease.

144. The vaccine of claim 142, wherein said neoplastic disease is selected from the group consisting of breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal cancer and osteogenic sarcoma.

145. The vaccine of claim 144, wherein said neoplastic disease is melanoma.

146. The vaccine of claim 134, wherein said protein of interest is melanoma antigen p15 (SEQ ID NO:212).

147. The vaccine of claim 127, wherein said OSPF-associated disorder is a state of toxicity due to a toxin.

148. The vaccine of claim 147, wherein said toxin is selected from the group consisting of botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin, aconotoxin, snake venom, scorpion venom and spider venoms.

149. The vaccine of claim 148, wherein said toxin is pertussis.

150. The vaccine of claim 134, wherein said protein of interest is pertussis toxin subunit 3 (SEQ ID NO:230).

151. The method of claim 127, wherein said OSPF-associated disorder is a parasitic infection due to a parasite.

152. The method of claim 151, wherein said parasite is selected from the group consisting of Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptospondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse, Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris.

153. The vaccine of claim 152, wherein said parasite is Plasmodium.

154. The method of claim 134, wherein said protein of interest is circumsporozoite protein II (SEQ ID NO:224).

155. A kit for immunizing a subject against an OSPF-associated disorder comprising the vaccine of any one of claims 98 or 127 and instructions for use.

156. A method of preventing an OSPF-associated disorder in a subject comprising administering to a subject an effective amount of an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, and wherein at least one single chain peptide overlaps with another single chain peptide by a length of Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by

a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is prevented in said subject.

157. The method of claim 156, wherein said subject is a vertebrate.

158. The method of claim 156, wherein said Y is fifteen (15) amino acids.

159. The method of claim 156, wherein said Z is five (5) amino acids.

160. The method of claim 156, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

161. The method of claim 160, wherein said MHC Class I-bearing cell is a CTL.

162. The method of claim 156, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

163. The method of claim 162, wherein said MHC Class II-bearing cell is a B cell.

164. The method of claim 156, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID

NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

165. The method of claim 156, wherein said OSPF-associated disorder is a viral infection due to a virus.

166. The method of claim 165, wherein said virus is selected from the group consisting of HIV, *e.g.*, HIV-1 and HIV-2, human herpes viruses, cytomegalovirus (esp Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, Ebola virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18 and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus..

167. The method of claim 166, wherein said virus is Ebola virus.

168. The method of claim 164, wherein said protein of interest is Ebola virus nucleoprotein (SEQ ID NO:210).

169. The method of claim 156, wherein said OSPF-associated disorder is a bacterial infection due to a bacteria.

170. The method of claim 169, wherein said bacteria is selected from the group consisting of N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H. influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis;

Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S. typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii; Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae.

171. The method of claim 170, wherein said bacteria is B. anthracis.

172. The method of claim 164, wherein said protein of interest is anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209).

173. The method of claim 156, wherein said OSPF-associated disorder is a neoplastic disease.

174. The method of claim 173, wherein said neoplastic disease is selected from the group consisting of breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal cancer and osteogenic sarcoma.

175. The method of claim 174, wherein said neoplastic disease is melanoma.

176. The method of claim 164, wherein said protein of interest is melanoma antigen p15 (SEQ ID NO:212);

177. The method of claim 156, wherein said OSPF-associated disorder is a state of toxicity due to a toxin.

178. The method of claim 177, wherein said toxin is selected from the group consisting of botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin, aconotoxin, snake venom, scorpion venom and spider venoms.

179. The method of claim 178, wherein said toxin is pertussis.

180. The method of claim 164, wherein said protein of interest is pertussis toxin subunit 3 (SEQ ID NO:230).

181. The method of claim 156, wherein said OSPF-associated disorder is a parasitic infection due to a parasite.

182. The method of claim 181, wherein said parasite is selected from the group consisting of Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptospondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse, Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris.

183. The method of claim 182, wherein said parasite is Plasmodium.

184. The method of claim 164, wherein said protein of interest is circumsporozoite protein II (SEQ ID NO:224).

185. A method of preventing an OSPF-associated disorder in a subject comprising administering to a subject an effective amount of an overlapping synthetic peptide

formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides is such that internalization of said single chain peptide by a MHC -bearing cell and presentation by a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is prevented in said subject.

186. The method of claim 185, wherein said subject is a vertebrate.

187. The method of claim 185, wherein said Y is fifteen (15) amino acids.

188. The method of claim 185, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

189. The method of claim 188, wherein said MHC Class I-bearing cell is a CTL.

190. The method of claim 185, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

191. The method of claim 190, wherein said MHC Class II-bearing cell is a B cell.

192. The method of claim 185, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222); circumsporozoite protein

precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

193. The method of claim 185, wherein said OSPF-associated disorder is a viral infection due to a virus.

194. The method of claim 193, wherein said virus is selected from the group consisting of HIV, *e.g.*, HIV-1 and HIV-2, human herpes viruses, cytomegalovirus ((esp Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, Ebola virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18 and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus.

195. The method of claim 194, wherein said virus is Ebola virus.

196. The method of claim 192, wherein said protein of interest is Ebola virus nucleoprotein (SEQ ID NO:210).

197. The method of claim 185, wherein said OSPF-associated disorder is a bacterial infection due to a bacteria.

198. The method of claim 197, wherein said bacteria is selected from the group consisting of N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H. influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including

M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis; Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S. typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii; Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae.

199. The method of claim 198, wherein said bacteria is B. anthracis.

200. The method of claim 192, wherein said protein of interest is anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209).

201. The method of claim 185, wherein said OSPF-associated disorder is a neoplastic disease.

202. The method of claim 201, wherein said neoplastic disease is selected from the group consisting of breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal cancer and osteogenic sarcoma.

203. The method of claim 202, wherein said neoplastic disease is melanoma.

204. The method of claim 192, wherein said protein of interest is melanoma antigen p15 (SEQ ID NO:212).

205. The method of claim 185, wherein said OSPF-associated disorder is a state of toxicity due to a toxin.

206. The method of claim 205, wherein said toxin is selected from the group consisting of botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin, aconotoxin, snake venom, scorpion venom and spider venoms.

207. The method of claim 206, wherein said toxin is pertussis.

208. The method of claim 192, wherein said protein of interest is pertussis toxin subunit 3 (SEQ ID NO:230).

209. The method of claim 185, wherein said OSPF-associated disorder is a parasitic infection due to a parasite.

210. The method of claim 209, wherein said parasite is selected from the group consisting of Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptospondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse, Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris.

211. The method of claim 210, wherein said parasite is Plasmodium.

212. The method of claim 192, wherein said protein of interest is selected from the group consisting of circumsporozoite protein precursor (SEQ ID NO:223) and circumsporozoite protein II (SEQ ID NO:224).

213. The method of any one of claims 1, 14, 43 70, 156 or 185 further comprising an adjuvant.

214. The method of claim 213, wherein said adjuvant is selected from the group consisting of interleukin (IL)-2, IL-12, IL-15, Freund's adjuvant, corynebacterium parvum and alum.

215. An adjuvant for a vaccine comprising a pharmaceutically acceptable carrier and an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptide is a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, and wherein at least one single chain peptide overlaps with another single chain peptide by a length of Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC -bearing cell and presentation by a MHC molecule to a T cell is possible.

216. A adjuvant for a vaccine comprising a pharmaceutically acceptable carrier and an overlapping synthetic peptide formulation (OSPF), wherein said OSPF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides is such that internalization of said single chain peptide by a MHC -bearing cell and presentation by a MHC molecule to a T cell is possible.

217. A method of modulating an immune response comprising contacting a cell with an overlapping synthetic peptide formulation (OPSF) wherein said OPSF

comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein at least one single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said immune response is modulated.

218. A method of modulating an immune response comprising contacting a cell with an overlapping synthetic peptide formulation (OPSF) wherein said OPSF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides are such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said immune response is modulated.

219. A method of treating an OSPF-associated disorder comprising contacting a cell with an overlapping synthetic peptide formulation (OPSF) wherein said OPSF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein at least one single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is treated.

220. A method of treating an OSPF-associated disorder comprising contacting a cell with an overlapping synthetic peptide formulation (OPSF) wherein said OPSF comprises a combination of single chain peptides corresponding to an amino acid

sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides are such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is treated.

221. A method of preventing an OSPF-associated disorder comprising contacting a cell with an overlapping synthetic peptide formulation (OPSF) wherein said OPSF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein at least one single chain peptide overlaps with another single chain peptide by a length represented by Z, wherein Z is 1 to (Y-1), wherein said length of said single chain peptide is such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is prevented.

222. A method of preventing an OSPF-associated disorder comprising contacting a cell with an overlapping synthetic peptide formulation (OPSF) wherein said OPSF comprises a combination of single chain peptides corresponding to an amino acid sequence of a protein of interest, wherein said single chain peptides are a length represented by Y, wherein Y is at least 7 to (X-1) and X is the number of amino acids of said protein of interest, wherein said length of said single chain peptides are such that internalization of said single chain peptide by a MHC-bearing cell and presentation by a MHC molecule to a T cell is possible, such that said OSPF-associated disorder is prevented.

223. The method of claims 217-222, wherein said Y is fifteen (15) amino acids.

224. The method of claims 217, 219 and 221, wherein said Z is five (5) amino acids.

225. The method of claims 217-222, wherein said immune response is a Th1-mediated immune response.

226. The method of claim 225, wherein said Th1-mediated immune response is a CTL-mediated immune response.

227. The method of claims 217-222, wherein said immune response is a Th2-mediated immune response.

228. The method of claim 227, wherein said Th2-mediated immune response is an antibody-associated immune response.

229. The method of claims 217-222, wherein said MHC-bearing cell is a MHC Class I-bearing cell.

230. The method of claim 229, wherein said MHC Class I-bearing cell is a CTL

231. The method of claims 217-222, wherein said MHC-bearing cell is a MHC Class II-bearing cell.

232. The method of claims 231, wherein said MHC Class II-bearing cell is a B cell.

233. The method of claims 217-222, wherein said protein of interest is selected from the group consisting of HIV Gag protein (SEQ ID NO:339); SIV Envelope protein (SEQ ID NO:340); anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209); Ebola virus nucleoprotein (SEQ ID NO:210); hepatitis C virus (HCV) polyprotein (SEQ ID NO:211); melanoma antigen p15 (SEQ ID NO:212); human Her2/neu protein (SEQ ID NO:213); respiratory syncytial virus (RSV) fusion protein (SEQ ID NO:214); HIV-2 gp41 protein (SEQ ID NO:215); HIV-2 GAG protein (SEQ ID NO:216); HIV-2 envelope (env) protein (SEQ ID NO:217); HIV-1 vpu protein (SEQ ID NO:218); HIV-1 envelope (env) protein (SEQ ID NO: 219); HIV-1 Tat interactive protein 2 (SEQ ID NO:220); HIV-1 reverse transcriptase (SEQ ID NO:221) and HIV-1 nef protein (SEQ ID NO:222);

circumsporozoite protein precursor (SEQ ID NO:223); circumsporozoite protein II (SEQ ID NO:224); pertussis-like toxin subunit (SEQ ID NO:225); S. aureus enterotoxin A (SEQ ID NO:226); E. coli enterotoxin A (SEQ ID NO:227); C. difficile enterotoxin A (SEQ ID NO:228); B. cereus enterotoxin A (SEQ ID NO:229); pertussis toxin subunit 3 (SEQ ID NO:230) ); SARS coronavirus (Frankfurt 1) envelope protein E (SEQ ID No:231); Human metapneumovirus fusion protein (SEQ ID NO:232); SARS coronavirus matrix protein (SEQ ID NO: 233); coronavirus nucleocapsid protein (SEQ ID NO: 234); and SARS coronavirus (Frankfurt 1) spike protein S (SEQ ID NO: 235).

234. The method of claims 219-222, wherein said OSPF-associated disorder is a viral infection due to a virus.

235. The method of claim 234, wherein said virus is selected from the group consisting of HIV, *e.g.*, HIV-1 and HIV-2, human herpes viruses, cytomegalovirus (esp. Human), Rotavirus, Epstein-Barr virus, Varicella Zoster Virus, hepatitis viruses, such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, paramyxoviruses: Respiratory Syncytial virus, parainfluenza virus, Ebola virus, measles virus, mumps virus, human papilloma viruses (for example HPV6, 11, 16, 18 and the like), flaviviruses (*e.g.* Yellow Fever Virus, Dengue Virus, Tick-borne encephalitis virus, Japanese Encephalitis Virus) or influenza virus.

236. The method of claim 235, wherein said virus is Ebola virus.

237. The method of claims 217-222, wherein said protein of interest is Ebola virus nucleoprotein (SEQ ID NO:210).

238. The method of claims 219-222, wherein said OSPF-associated disorder is a bacterial infection due toa bacteria.

239. The method of claim 238, wherein said bacteria is selected from the group consisting of N. gonorrhea and N. meningitidis, Streptococcus spp, including S. pneumoniae, S. pyogenes, S. agalactiae, S. mutans; Haemophilus spp, including H.

influenzae type B, non typeable H. influenzae, H. ducreyi; Moraxella spp, including M catarrhalis, also known as Branhamella catarrhalis; Bordetella spp, including B. pertussis, B. parapertussis and B. bronchiseptica; Mycobacterium spp., including M. tuberculosis, M. bovis, M. leprae, M. avium, M. paratuberculosis, M. smegmatis; Legionella spp, including L. pneumophila; Escherichia spp, including enterotoxic E. coli, enterohemorragic E. coli, enteropathogenic E. coli; Vibrio spp, including V. cholera, Shigella spp, including S. sonnei, S. dysenteriae, S. flexnerii; Yersinia spp, including Y. enterocolitica, Y. pestis, Y. pseudotuberculosis, Campylobacter spp, including C. jejuni and C. coli; Salmonella spp, including S. typhi, S. paratyphi, S. choleraesuis, S. enteritidis; Listeria spp., including L. monocytogenes; Helicobacter spp, including H. pylori; Pseudomonas spp, including P. aeruginosa, Staphylococcus spp., including S. aureus, S. epidermidis; Enterococcus spp., including E. faecalis, E. faecium; Clostridium spp., including C. tetani, C. botulinum, C. difficile; Bacillus spp., including B. anthracis; Corynebacterium spp., including C. diphtheriae; Borrelia spp., including B. burgdorferi, B. garinii, B. afzelii, B. andersonii, B. hermsii; Ehrlichia spp., including E. equi and the agent of the Human Granulocytic Ehrlichiosis; Rickettsia spp, including R. rickettsii; Chlamydia spp., including C. trachomatis, C. neumoniae, C. psittaci; Leptira spp., including L. interrogans; Treponema spp., including T. pallidum, T. denticola, T. hyodysenteriae.

240. The method of claim 239, wherein said bacteria is B. anthracis.

241. The method of claims 217-222, wherein said protein of interest is anthrax toxins translocating protein (protective antigen precursor [PA]) (SEQ ID NO:209).

242. The method of claims 219-222, wherein said OSPF-associated disorder is a neoplastic disease.

243. The method of claim 242, wherein said neoplastic disease is selected from the group consisting of breast, colon, non-small cell lung, head and neck, colorectal, lung, prostate, ovary, renal, melanoma, gastrointestinal cancer and osteogenic sarcoma.

244. The method of claim 243, wherein said neoplastic disease is melanoma.

245. The method of claims 217-222, wherein said protein of interest is melanoma antigen p15 (SEQ ID NO:212).

246. The method of claims 219-222, wherein said OSPF-associated disorder is a state of toxicity due to a toxin.

247. The method of claim 246, wherein said toxin is selected from the group consisting of botulin, perfringens toxin, pertussis, mycotoxins, shigatoxins, staphylococcal enterotoxin B, tetanus, ricin, cholera, aflatoxins, diphtheria, T2, seguitoxin, saxitoxin, abrin, cyanoginosin, alphatoxin, tetrodotoxin, aconotoxin, snake venom, scorpion venom and spider venoms.

248. The method of claim 246, wherein said toxin is pertussis.

249. The method of claims 217-222, wherein said protein of interest is pertussis toxin subunit 3 (SEQ ID NO:230).

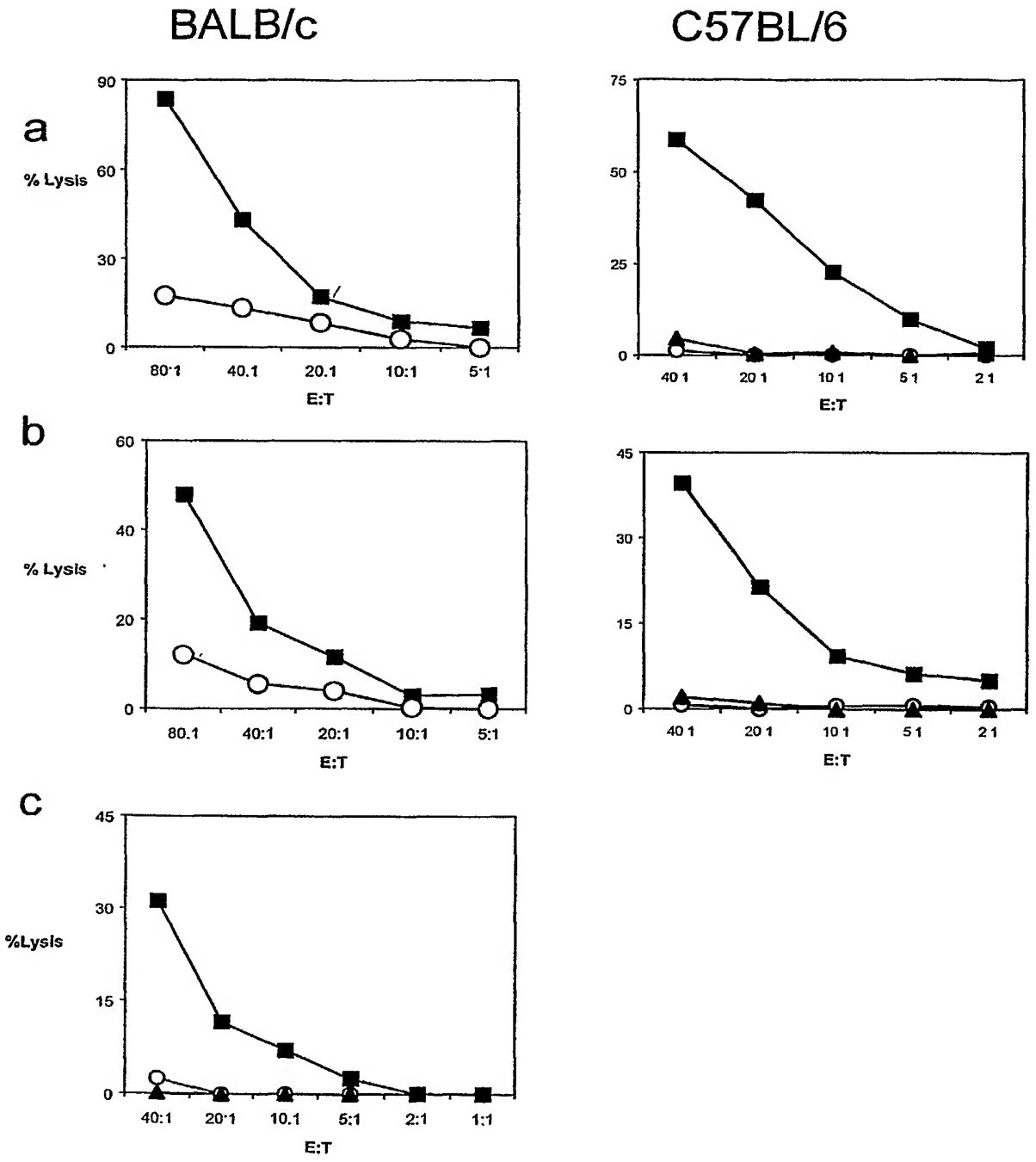
250. The method of claims 219-222, wherein said OSPF-associated disorder is a parasitic infection due to a parasite.

251. The method of claim 250, wherein said parasite is selected from the group consisting of Anaplasma, Babesia, Balantidium, Besnoitia, Chlamydia, Coccidia, Cryptosondium, Cytauxzoon, Eimeria Entamoeba, Eperythrozoon, Erlichia, Giardia, Haemobartonella, Hammondia, Isopora, Leishmania, Neorickettsia, Plasmodium, Pneumocystis, Rickettsia, Schistosoma, Sarcocystis, Theileria, Thrichinella, Toxoplasma, Trichomonas, Trypanosoma, Unicaria, Dipylidium, Echinococcuse, Taenia, Ancylostoma, Ascaris, Enterobius, Strongyloides, Strongylus, Toxocara, Toxascaris and Trichuris.

252. The method of claim 251, wherein said parasite is Plasmodium.

253. The method of claims 217-222, wherein said protein of interest is circumsporozoite protein II (SEQ ID NO:224).

# Fig. 1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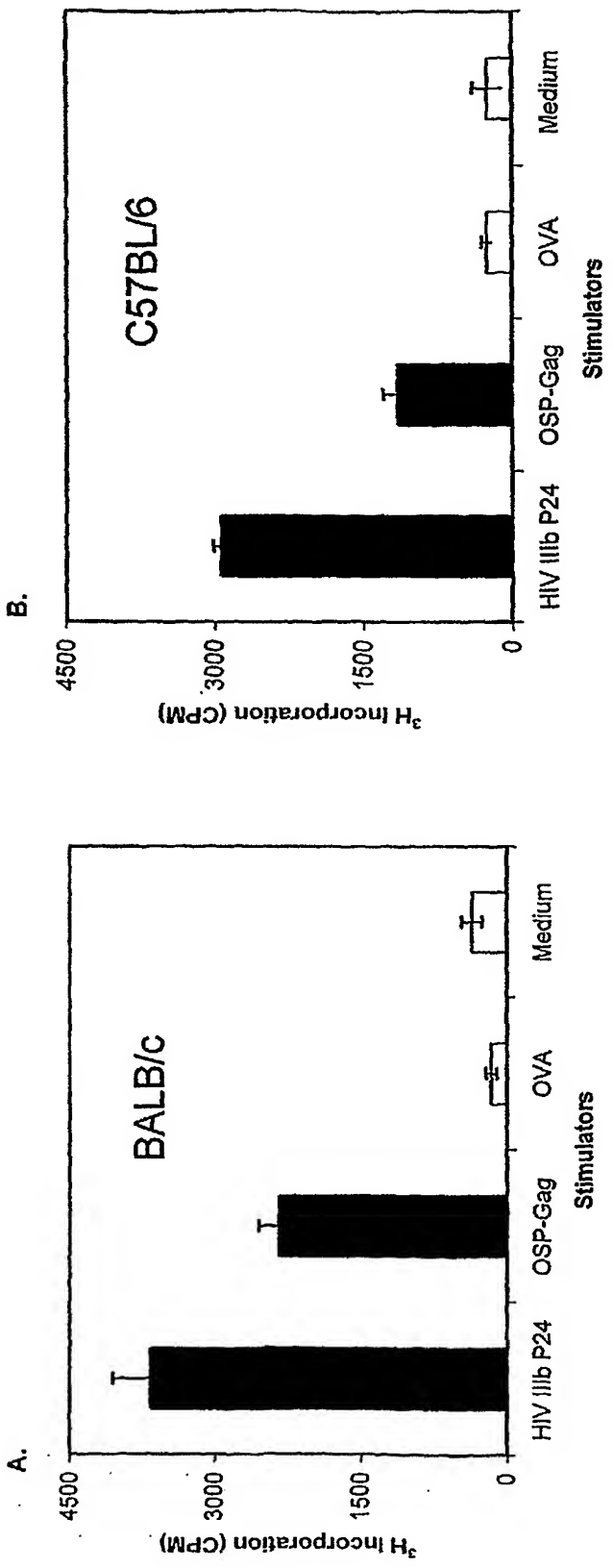
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Fig. 2

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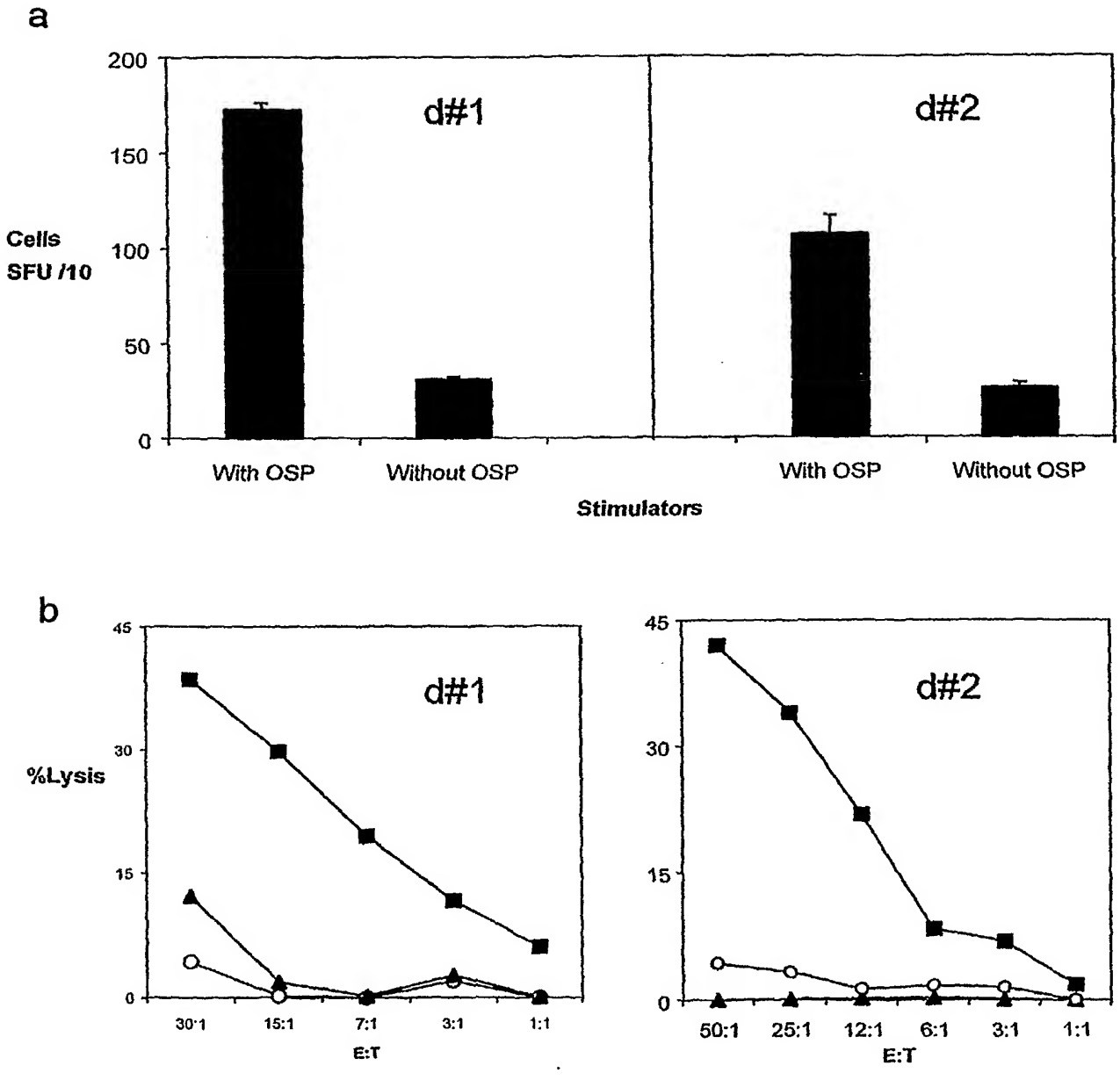
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SEQUENCE LISTING

<110> Dana-Farber Cancer Institute, Inc., et al.

<120> COMPOSITIONS AND METHODS FOR MODULATING
A CYTOTOXIC T LYMPHOCYTE IMMUNE RESPONSE

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<400> 51
Leu Lys Glu Thr Ile Asn Glu Glu Ala Ala Glu Trp Asp Arg Val
1 5 10 15

<210> 52
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<400> 52
Ile Asn Glu Glu Ala Ala Glu Trp Asp Arg Val His Pro Val His
1 5 10 15

<210> 53
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<213> Human Immunodeficiency Virus

<400> 53
Ala Ala Glu Trp Asp Arg Val His Pro Val His Ala Gly Pro Ile
1 5 10 15

<210> 54
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<400> 54
Asp Arg Val His Pro Val His Ala Gly Pro Ile Ala Pro Gly Gln
1 5 10 15

<210> 55
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<400> 55
Pro Val His Ala Gly Pro Ile Ala Pro Gly Gln Met Arg Glu Pro
1 5 10 15

<210> 56
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<400> 56
Gly Pro Ile Ala Pro Gly Gln Met Arg Glu Pro Arg Gly Ser Asp

1 5 10 15

<210> 57
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<213> Human Immunodeficiency Virus

<400> 57
Pro Gly Gln Met Arg Glu Pro Arg Gly Ser Asp Ile Ala Gly Thr
1 5 10 15

<210> 58
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<400> 58
Arg Glu Pro Arg Gly Ser Asp Ile Ala Gly Thr Thr Ser Thr Leu
1 5 10 15

<210> 59
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<400> 59
Gly Ser Asp Ile Ala Gly Thr Thr Ser Thr Leu Gln Glu Gln Ile
1 5 10 15

<210> 60
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<400> 60
Ala Gly Thr Thr Ser Thr Leu Gln Glu Gln Ile Gly Trp Met Thr
1 5 10 15

<210> 61
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<400> 61
Ser Thr Leu Gln Glu Gln Ile Gly Trp Met Thr Asn Asn Pro Pro
1 5 10 15

<210> 62
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<213> Human Immunodeficiency Virus

<400> 62
Glu Gln Ile Gly Trp Met Thr Asn Asn Pro Pro Ile Pro Val Gly
1 5 10 15

<210> 63
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<400> 63
Trp Met Thr Asn Asn Pro Pro Ile Pro Val Gly Glu Ile Tyr Lys
1 5 10 15

<210> 64
<211> 15
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<213> Human Immunodeficiency Virus

<400> 64
Asn Pro Pro Ile Pro Val Gly Glu Ile Tyr Lys Arg Trp Ile Ile
1 5 10 15

<210> 65
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<400> 65
Pro Val Gly Glu Ile Tyr Lys Arg Trp Ile Ile Leu Gly Leu Asn
1 5 10 15

<210> 66

<211> 15
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<400> 66
Ile Tyr Lys Arg Trp Ile Ile Leu Gly Leu Asn Lys Ile Val Arg
1 5 10 15

<210> 67
<211> 15
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<213> Human Immunodeficiency Virus

<400> 67
Trp Ile Ile Leu Gly Leu Asn Lys Ile Val Arg Met Tyr Ser Pro
1 5 10 15

<210> 68
<211> 15
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<213> Human Immunodeficiency Virus

<400> 68
Gly Leu Asn Lys Ile Val Arg Met Tyr Ser Pro Thr Ser Ile Leu
1 5 10 15

<210> 69
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<213> Human Immunodeficiency Virus

<400> 69
Ile Val Arg Met Tyr Ser Pro Thr Ser Ile Leu Asp Ile Arg Gln
1 5 10 15

<210> 70
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<400> 70
Tyr Ser Pro Thr Ser Ile Leu Asp Ile Arg Gln Gly Pro Lys Glu
1 5 10 15

<210> 71
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<400> 71
Ser Ile Leu Asp Ile Arg Gln Gly Pro Lys Glu Pro Phe Arg Asp
1 5 10 15

<210> 72
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<212> PRT
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<400> 72
Ile Arg Gln Gly Pro Lys Glu Pro Phe Arg Asp Tyr Val Asp Arg
1 5 10 15

<210> 73
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<213> Human Immunodeficiency Virus

<400> 73
Pro Lys Glu Pro Phe Arg Asp Tyr Val Asp Arg Phe Tyr Lys Thr
1 5 10 15

<210> 74
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<213> Human Immunodeficiency Virus

<400> 74
Phe Arg Asp Tyr Val Asp Arg Phe Tyr Lys Thr Leu Arg Ala Glu
1 5 10 15

<210> 75
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<213> Human Immunodeficiency Virus

<400> 75
Val Asp Arg Phe Tyr Lys Thr Leu Arg Ala Glu Gln Ala Ser Gln
1 5 10 15

<210> 76
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 76
Tyr Lys Thr Leu Arg Ala Glu Gln Ala Ser Gln Glu Val Lys Asn
1 5 10 15

<210> 77
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 77
Arg Ala Glu Gln Ala Ser Gln Glu Val Lys Asn Trp Met Thr Glu
1 5 10 15

<210> 78
<211> 15
<212> PRT

<213> Human Immunodeficiency Virus

<400> 78
Ala Ser Gln Glu Val Lys Asn Trp Met Thr Glu Thr Leu Leu Val
1 5 10 15

<210> 79

<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 79
Val Lys Asn Trp Met Thr Glu Thr Leu Leu Val Gln Asn Ala Asn
1 5 10 15

<210> 80
<211> 15
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<213> Human Immunodeficiency Virus

<400> 80
Met Thr Glu Thr Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys
1 5 10 15

<210> 81
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 81
Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Thr Ile Leu Lys
1 5 10 15

<210> 82
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 82
Asn Ala Asn Pro Asp Cys Lys Thr Ile Leu Lys Ala Leu Gly Pro
1 5 10 15

<210> 83
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 83
Asp Cys Lys Thr Ile Leu Lys Ala Leu Gly Pro Ala Ala Thr Leu
1 5 10 15

<210> 84
<211> 15
<212> PRT

<213> Human Immunodeficiency Virus

<400> 84
Ile Leu Lys Ala Leu Gly Pro Ala Ala Thr Leu Glu Glu Met Met
1 5 10 15

<210> 85
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 85
Leu Gly Pro Ala Ala Thr Leu Glu Glu Met Met Thr Ala Cys Gln
1 5 10 15

<210> 86
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 86
Ala Thr Leu Glu Glu Met Met Thr Ala Cys Gln Gly Val Gly Gly
1 5 10 15

<210> 87
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 87
Glu Met Met Thr Ala Cys Gln Gly Val Gly Gly Pro Gly His Lys
1 5 10 15

<210> 88
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 88
Ala Cys Gln Gly Val Gly Gly Pro Gly His Lys Ala Arg Val Leu
1 5 10 15

<210> 89
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 89
Val Gly Gly Pro Gly His Lys Ala Arg Val Leu Ala Glu Ala Met
1 5 10 15

<210> 90
<211> 15
<212> PRT

<213> Human Immunodeficiency Virus

<400> 90
Gly His Lys Ala Arg Val Leu Ala Glu Ala Met Ser Gln Val Thr
1 5 10 15

<210> 91
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 91
Arg Val Leu Ala Glu Ala Met Ser Gln Val Thr Asn Ser Ala Thr
1 5 10 15

<210> 92
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 92
Glu Ala Met Ser Gln Val Thr Asn Ser Ala Thr Ile Met Met Gln
1 5 10 15

<210> 93
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 93
Gln Val Thr Asn Ser Ala Thr Ile Met Met Gln Arg Gly Asn Phe
1 5 10 15

<210> 94
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 94
Ser Ala Thr Ile Met Met Gln Arg Gly Asn Phe Arg Asn Gln Arg
1 5 10 15

<210> 95
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 95
Met Met Gln Arg Gly Asn Phe Arg Asn Gln Arg Lys Ile Val Lys
1 5 10 15

<210> 96
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 96
Gly Asn Phe Arg Asn Gln Arg Lys Ile Val Lys Cys Phe Asn Cys
1 5 10 15

<210> 97
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 97
Asn Gln Arg Lys Ile Val Lys Cys Phe Asn Cys Gly Lys Glu Gly
1 5 10 15

<210> 98
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 98
Ile Val Lys Cys Phe Asn Cys Gly Lys Glu Gly His Thr Ala Arg
1 5 10 15

<210> 99
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 99
Phe Asn Cys Gly Lys Glu Gly His Thr Ala Arg Asn Cys Arg Ala
1 5 10 15

<210> 100
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 100
Lys Glu Gly His Thr Ala Arg Asn Cys Arg Ala Pro Arg Lys Lys
1 5 10 15

<210> 101
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 101
Thr Ala Arg Asn Cys Arg Ala Pro Arg Lys Lys Gly Cys Trp Lys
1 5 10 15

<210> 102
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 102
Cys Arg Ala Pro Arg Lys Lys Gly Cys Trp Lys Cys Gly Lys Glu
1 5 10 15

<210> 103
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 103
Arg Lys Lys Gly Cys Trp Lys Cys Gly Lys Glu Gly His Gln Met
1 5 10 15

<210> 104
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 104
Cys Trp Lys Cys Gly Lys Glu Gly His Gln Met Lys Asp Cys Thr
1 5 10 15

<210> 105
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 105
Gly Lys Glu Gly His Gln Met Lys Asp Cys Thr Glu Arg Gln Ala
1 5 10 15

<210> 106
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 106
His Gln Met Lys Asp Cys Thr Glu Arg Gln Ala Asn Phe Leu Gly
1 5 10 15

<210> 107
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 107
Asp Cys Thr Glu Arg Gln Ala Asn Phe Leu Gly Lys Ile Trp Pro
1 5 10 15

<210> 108
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 108
Arg Gln Ala Asn Phe Leu Gly Lys Ile Trp Pro Ser Tyr Lys Gly
1 5 10 15

<210> 109
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 109
Phe Leu Gly Lys Ile Trp Pro Ser Tyr Lys Gly Arg Pro Gly Asn
1 5 10 15

<210> 110
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 110
Ile Trp Pro Ser Tyr Lys Gly Arg Pro Gly Asn Phe Leu Gln Ser
1 5 10 15

<210> 111
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 111
Tyr Lys Gly Arg Pro Gly Asn Phe Leu Gln Ser Arg Pro Glu Pro
1 5 10 15

<210> 112
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 112
Pro Gly Asn Phe Leu Gln Ser Arg Pro Glu Pro Thr Ala Pro Pro
1 5 10 15

<210> 113
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 113
Leu Gln Ser Arg Pro Glu Pro Thr Ala Pro Pro Glu Glu Ser Phe
1 5 10 15

<210> 114
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 114

Pro Glu Pro Thr Ala Pro Pro Glu Glu Ser Phe Arg Ser Gly Val
1 5 10 15

<210> 115
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 115
Ala Pro Pro Glu Glu Ser Phe Arg Ser Gly Val Glu Thr Thr Thr
1 5 10 15

<210> 116
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 116
Glu Ser Phe Arg Ser Gly Val Glu Thr Thr Thr Pro Pro Gln Lys
1 5 10 15

<210> 117
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 117
Ser Gly Val Glu Thr Thr Thr Pro Pro Gln Lys Gln Glu Pro Ile
1 5 10 15

<210> 118
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 118
Thr Thr Thr Pro Pro Gln Lys Gln Glu Pro Ile Asp Lys Glu Leu
1 5 10 15

<210> 119
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 119
Pro Gln Lys Gln Glu Pro Ile Asp Lys Glu Leu Tyr Pro Leu Thr
1 5 10 15

<210> 120
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 120
Glu Pro Ile Asp Lys Glu Leu Tyr Pro Leu Thr Ser Leu Arg Ser

1 5 10 15

<210> 121
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 121
Lys Glu Leu Tyr Pro Leu Thr Ser Leu Arg Ser Leu Phe Gly Asn
1 5 10 15

<210> 122
<211> 16
<212> PRT
<213> Human Immunodeficiency Virus

<400> 122
Pro Leu Thr Ser Leu Arg Ser Leu Phe Gly Asn Asp Pro Ser Ser Gln
1 5 10 15

<210> 123
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 123
Met Gly Cys Leu Gly Asn Gln Leu Leu Ile Ala Ile Leu Leu Leu Ser
1 5 10 15
Val Tyr Gly Ile
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<210> 124
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 124
Ala Ile Leu Leu Leu Ser Val Tyr Gly Ile Tyr Cys Thr Leu Tyr Val
1 5 10 15
Thr Val Phe Tyr
20

<210> 125
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 125
Tyr Cys Thr Leu Tyr Val Thr Val Phe Tyr Gly Val Pro Ala Trp Arg
1 5 10 15
Asn Ala Thr Ile
20

<210> 126

<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 126
Gly Val Pro Ala Trp Arg Asn Ala Thr Ile Pro Leu Phe Cys Ala Thr
1 5 10 15
Lys Asn Arg Asp
20

<210> 127
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 127
Pro Leu Phe Cys Ala Thr Lys Asn Arg Asp Thr Trp Gly Thr Thr Gln
1 5 10 15
Cys Leu Pro Asp
20

<210> 128
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 128
Thr Trp Gly Thr Thr Gln Cys Leu Pro Asp Asn Gly Asp Tyr Ser Glu
1 5 10 15
Val Ala Leu Asn
20

<210> 129
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 129
Asn Gly Asp Tyr Ser Glu Val Ala Leu Asn Val Thr Glu Ser Phe Asp
1 5 10 15
Ala Trp Asn Asn
20

<210> 130
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 130
Val Thr Glu Ser Phe Asp Ala Trp Asn Asn Thr Val Thr Glu Gln Ala
1 5 10 15
Ile Glu Asp Val
20

<210> 131
<211> 20

<212> PRT
<213> Simian Immunodeficiency Virus

<400> 131
Thr Val Thr Glu Gln Ala Ile Glu Asp Val Trp Gln Leu Phe Glu Thr
1 5 10 15
Ser Ile Lys Pro
20

<210> 132
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 132
Trp Gln Leu Phe Glu Thr Ser Ile Lys Pro Cys Val Lys Leu Ser Pro
1 5 10 15
Leu Cys Ile Thr
20

<210> 133
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 133
Cys Val Lys Leu Ser Pro Leu Cys Ile Thr Met Arg Cys Asn Lys Ser
1 5 10 15
Glu Thr Asp Arg
20

<210> 134
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 134
Met Arg Cys Asn Lys Ser Glu Thr Asp Arg Trp Gly Leu Thr Lys Ser
1 5 10 15
Ile Thr Thr Thr
20

<210> 135
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 135
Trp Gly Leu Thr Lys Ser Ile Thr Thr Thr Ala Ser Thr Thr Ser Thr
1 5 10 15
Thr Ala Ser Ala
20

<210> 136
<211> 20
<212> PRT

<213> Simian Immunodeficiency Virus

<400> 136
Ala Ser Thr Thr Ser Thr Thr Ala Ser Ala Lys Val Asp Met Val Asn
1 5 10 15
Glu Thr Ser Ser
20

<210> 137
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 137
Lys Val Asp Met Val Asn Glu Thr Ser Ser Cys Ile Ala Gln Asp Asn
1 5 10 15
Cys Thr Gly Leu
20

<210> 138
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 138
Cys Ile Ala Gln Asp Asn Cys Thr Gly Leu Glu Gln Glu Gln Met Ile
1 5 10 15
Ser Cys Lys Phe
20

<210> 139
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 139
Glu Gln Glu Gln Met Ile Ser Cys Lys Phe Asn Met Thr Gly Leu Lys
1 5 10 15
Arg Asp Lys Lys
20

<210> 140
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 140
Asn Met Thr Gly Leu Lys Arg Asp Lys Lys Lys Glu Tyr Asn Glu Thr
1 5 10 15
Trp Tyr Ser Ala
20

<210> 141
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 141
Lys Glu Tyr Asn Glu Thr Trp Tyr Ser Ala Asp Leu Val Cys Glu Gln
1 5 10 15
Gly Asn Asn Thr
20

<210> 142
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 142
Asp Leu Val Cys Glu Gln Gly Asn Asn Thr Gly Asn Glu Ser Arg Cys
1 5 10 15
Tyr Met Asn His
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<210> 143
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 143
Gly Asn Glu Ser Arg Cys Tyr Met Asn His Cys Asn Thr Ser Val Ile
1 5 10 15
Gln Glu Ser Cys
20

<210> 144
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 144
Cys Asn Thr Ser Val Ile Gln Glu Ser Cys Asp Lys His Tyr Trp Asp
1 5 10 15
Ala Ile Arg Phe
20

<210> 145
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 145
Asp Lys His Tyr Trp Asp Ala Ile Arg Phe Arg Tyr Cys Ala Pro Pro
1 5 10 15
Gly Tyr Ala Leu
20

<210> 146
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 146
Arg Tyr Cys Ala Pro Pro Gly Tyr Ala Leu Leu Arg Cys Asn Asp Thr
1 5 10 15
Asn Tyr Ser Gly
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<210> 147
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 147
Leu Arg Cys Asn Asp Thr Asn Tyr Ser Gly Phe Met Pro Lys Cys Ser
1 5 10 15
Lys Val Val Val
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<210> 148
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 148
Phe Met Pro Lys Cys Ser Lys Val Val Val Ser Ser Cys Thr Arg Met
1 5 10 15
Met Glu Thr Gln
20

<210> 149
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 149
Ser Ser Cys Thr Arg Met Met Glu Thr Gln Thr Ser Thr Trp Phe Gly
1 5 10 15
Phe Asn Gly Thr
20

<210> 150
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 150
Thr Ser Thr Trp Phe Gly Phe Asn Gly Thr Arg Ala Glu Asn Arg Thr
1 5 10 15
Tyr Ile Tyr Trp
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<210> 151
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 151

Arg Ala Glu Asn Arg Thr Tyr Ile Tyr Trp His Gly Arg Asp Asn Arg
1 5 10 15
Thr Ile Ile Ser
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<210> 152
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 152
His Gly Arg Asp Asn Arg Thr Ile Ile Ser Leu Asn Lys Tyr Tyr Asn
1 5 10 15
Leu Thr Met Lys
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<210> 153
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 153
Leu Asn Lys Tyr Tyr Asn Leu Thr Met Lys Cys Arg Arg Pro Gly Asn
1 5 10 15
Lys Thr Val Leu
20

<210> 154
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 154
Cys Arg Arg Pro Gly Asn Lys Thr Val Leu Pro Val Thr Ile Met Ser
1 5 10 15
Gly Leu Val Phe
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<210> 155
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 155
Pro Val Thr Ile Met Ser Gly Leu Val Phe His Ser Gln Pro Ile Asn
1 5 10 15
Asp Arg Pro Lys
20

<210> 156
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 156
His Ser Gln Pro Ile Asn Asp Arg Pro Lys Gln Ala Trp Cys Trp Phe

1 5 10 15
Gly Gly Lys Trp
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<210> 157
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 157
Gln Ala Trp Cys Trp Phe Gly Gly Lys Trp Lys Asp Ala Ile Lys Glu
1 5 10 15
Val Lys Gln Thr
20

<210> 158
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 158
Lys Asp Ala Ile Lys Glu Val Lys Gln Thr Ile Val Lys His Pro Arg
1 5 10 15
Tyr Thr Gly Thr
20

<210> 159
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 159
Ile Val Lys His Pro Arg Tyr Thr Gly Thr Asn Asn Thr Asp Lys Ile
1 5 10 15
Asn Leu Thr Ala
20

<210> 160
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 160
Asn Asn Thr Asp Lys Ile Asn Leu Thr Ala Pro Gly Gly Gly Asp Pro
1 5 10 15
Glu Val Thr Phe
20

<210> 161
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 161

Pro Gly Gly Gly Asp Pro Glu Val Thr Phe Met Trp Thr Asn Cys Arg
1 5 10 15
Gly Glu Phe Leu
20

<210> 162
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 162
Met Trp Thr Asn Cys Arg Gly Glu Phe Leu Tyr Cys Lys Met Asn Trp
1 5 10 15
Phe Leu Asn Trp
20

<210> 163
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 163
Tyr Cys Lys Met Asn Trp Phe Leu Asn Trp Val Glu Asp Arg Asn Thr
1 5 10 15
Ala Asn Gln Lys
20

<210> 164
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 164
Val Glu Asp Arg Asn Thr Ala Asn Gln Lys Pro Lys Glu Gln His Lys
1 5 10 15
Arg Asn Tyr Val
20

<210> 165
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 165
Pro Lys Glu Gln His Lys Arg Asn Tyr Val Pro Cys His Ile Arg Gln
1 5 10 15
Ile Ile Asn Thr
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<210> 166
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 166
Pro Cys His Ile Arg Gln Ile Ile Asn Thr Trp His Lys Val Gly Lys

1 5 10 15
Asn Val Tyr Leu
20

<210> 167
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 167
Trp His Lys Val Gly Lys Asn Val Tyr Leu Pro Pro Arg Glu Gly Asp
1 5 10 15
Leu Thr Cys Asn
20

<210> 168
<211> 20
<212> PRT

<213> Simian Immunodeficiency Virus

<400> 168
Pro Pro Arg Glu Gly Asp Leu Thr Cys Asn Ser Thr Val Thr Ser Leu
1 5 10 15
Ile Ala Asn Ile
20

<210> 169
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 169
Ser Thr Val Thr Ser Leu Ile Ala Asn Ile Asp Trp Ile Asp Gly Asn
1 5 10 15
Gln Thr Asn Ile
20

<210> 170
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 170
Asp Trp Ile Asp Gly Asn Gln Thr Asn Ile Thr Met Ser Ala Glu Val
1 5 10 15
Ala Glu Leu Tyr
20

<210> 171
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 171
Thr Met Ser Ala Glu Val Ala Glu Leu Tyr Arg Leu Glu Leu Gly Asp

```
 1               5                   10                  15
Tyr Lys Leu Val
            20


<210> 172
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 172
Arg Leu Glu Leu Gly Asp Tyr Lys Leu Val Glu Ile Thr Pro Ile Gly
 1               5                   10                  15
Leu Ala Pro Thr
            20


<210> 173
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 173
Glu Ile Thr Pro Ile Gly Leu Ala Pro Thr Asp Val Lys Arg Tyr Thr
 1               5                   10                  15
Thr Gly Gly Thr
            20


<210> 174
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 174
Asp Val Lys Arg Tyr Thr Thr Gly Gly Thr Ser Arg Asn Lys Arg Gly
 1               5                   10                  15
Val Phe Val Leu
            20


<210> 175
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 175
Ser Arg Asn Lys Arg Gly Val Phe Val Leu Gly Phe Leu Gly Phe Leu
 1               5                   10                  15
Ala Thr Ala Gly
            20


<210> 176
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 176
Gly Phe Leu Gly Phe Leu Ala Thr Ala Gly Ser Ala Met Gly Ala Ala
 1               5                   10                  15
```

Ser Leu Thr Leu
20

<210> 177
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 177
Ser Ala Met Gly Ala Ala Ser Leu Thr Leu Thr Ala Gln Ser Arg Thr
1 5 10 15
Leu Leu Ala Gly
20

<210> 178
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 178
Thr Ala Gln Ser Arg Thr Leu Leu Ala Gly Ile Val Gln Gln Gln Gln
1 5 10 15
Gln Leu Leu Asp
20

<210> 179
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 179
Ile Val Gln Gln Gln Gln Gln Leu Leu Asp Val Val Lys Arg Gln Gln
1 5 10 15
Glu Leu Leu Arg
20

<210> 180
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 180
Val Val Lys Arg Gln Gln Glu Leu Leu Arg Leu Thr Val Trp Gly Thr
1 5 10 15
Lys Asn Leu Gln
20

<210> 181
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 181
Leu Thr Val Trp Gly Thr Lys Asn Leu Gln Thr Arg Val Thr Ala Ile
1 5 10 15
Glu Lys Tyr Leu

20

<210> 182
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 182
Thr Arg Val Thr Ala Ile Glu Lys Tyr Leu Lys Asp Gln Ala Gln Leu
1 5 10 15
Asn Ala Trp Gly
20

<210> 183
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 183
Lys Asp Gln Ala Gln Leu Asn Ala Trp Gly Cys Ala Phe Arg Gln Val
1 5 10 15
Cys His Thr Thr
20

<210> 184
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 184
Cys Ala Phe Arg Gln Val Cys His Thr Thr Val Pro Trp Pro Asn Ala
1 5 10 15
Ser Leu Thr Pro
20

<210> 185
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 185
Val Pro Trp Pro Asn Ala Ser Leu Thr Pro Lys Trp Asn Asn Glu Thr
1 5 10 15
Trp Gln Glu Trp
20

<210> 186
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 186
Lys Trp Asn Asn Glu Thr Trp Gln Glu Trp Glu Arg Lys Val Asp Phe
1 5 10 15
Leu Glu Glu Asn
20

<210> 187
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 187
Glu Arg Lys Val Asp Phe Leu Glu Glu Asn Ile Thr Ala Leu Leu Glu
1 5 10 15
Glu Ala Gln Ile
20

<210> 188
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 188
Ile Thr Ala Leu Leu Glu Glu Ala Gln Ile Gln Gln Glu Lys Asn Met
1 5 10 15
Tyr Glu Leu Gln
20

<210> 189
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 189
Gln Gln Glu Lys Asn Met Tyr Glu Leu Gln Lys Leu Asn Ser Trp Asp
1 5 10 15
Val Phe Gly Asn
20

<210> 190
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 190
Lys Leu Asn Ser Trp Asp Val Phe Gly Asn Trp Phe Asp Leu Ala Ser
1 5 10 15
Trp Ile Lys Tyr
20

<210> 191
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 191
Trp Phe Asp Leu Ala Ser Trp Ile Lys Tyr Ile Gln Tyr Gly Val Tyr
1 5 10 15
Ile Val Val Gly
20

<210> 192
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 192
Ile Gln Tyr Gly Val Tyr Ile Val Val Gly Val Ile Leu Leu Arg Ile
1 5 10 15
Val Ile Tyr Ile
20

<210> 193
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 193
Val Ile Leu Leu Arg Ile Val Ile Tyr Ile Val Gln Met Leu Ala Lys
1 5 10 15
Leu Arg Gln Gly
20

<210> 194
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 194
Val Gln Met Leu Ala Lys Leu Arg Gln Gly Tyr Arg Pro Val Phe Ser
1 5 10 15
Ser Pro Pro Ser
20

<210> 195
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 195
Tyr Arg Pro Val Phe Ser Ser Pro Pro Ser Tyr Phe Gln Gln Thr His
1 5 10 15
Ile Gln Gln Asp
20

<210> 196
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 196
Tyr Phe Gln Gln Thr His Ile Gln Gln Asp Pro Ala Leu Pro Thr Arg
1 5 10 15
Glu Gly Lys Glu
20

<210> 197
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 197
Pro Ala Leu Pro Thr Arg Glu Gly Lys Glu Arg Asp Gly Gly Glu Gly
1 5 10 15
Gly Gly Asn Ser
20

<210> 198
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 198
Arg Asp Gly Gly Glu Gly Gly Gly Asn Ser Ser Trp Pro Trp Gln Ile
1 5 10 15
Glu Tyr Ile His
20

<210> 199
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 199
Ser Trp Pro Trp Gln Ile Glu Tyr Ile His Phe Leu Ile Arg Gln Leu
1 5 10 15
Ile Arg Leu Leu
20

<210> 200
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 200
Phe Leu Ile Arg Gln Leu Ile Arg Leu Leu Thr Trp Leu Phe Ser Asn
1 5 10 15
Cys Arg Thr Leu
20

<210> 201
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 201
Thr Trp Leu Phe Ser Asn Cys Arg Thr Leu Leu Ser Arg Val Tyr Gln
1 5 10 15
Ile Leu Gln Pro
20

<210> 202

<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 202
Leu Ser Arg Val Tyr Gln Ile Leu Gln Pro Ile Leu Gln Arg Leu Ser
1 5 10 15
Ala Thr Leu Gln
20

<210> 203
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 203
Ile Leu Gln Arg Leu Ser Ala Thr Leu Gln Arg Ile Arg Glu Val Leu
1 5 10 15
Arg Thr Glu Leu
20

<210> 204
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 204
Arg Ile Arg Glu Val Leu Arg Thr Glu Leu Thr Tyr Leu Gln Tyr Gly
1 5 10 15
Trp Ser Tyr Phe
20

<210> 205
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 205
Thr Tyr Leu Gln Tyr Gly Trp Ser Tyr Phe His Glu Ala Val Gln Ala
1 5 10 15
Val Trp Arg Ser
20

<210> 206
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 206
His Glu Ala Val Gln Ala Val Trp Arg Ser Ala Thr Glu Thr Leu Ala
1 5 10 15
Gly Ala Trp Gly
20

<210> 207
<211> 9

<212> PRT
<213> Human Immunodeficiency Virus

<400> 207
Ala Met Gln Met Leu Lys Glu Thr Ile
1 5

<210> 208
<211> 9
<212> PRT
<213> Human Immunodeficiency Virus

<400> 208
Gly Pro Gly Gln Ala Phe Tyr Ala Thr
1 5

<210> 209
<211> 764
<212> PRT
<213> Bacillus anthracis

<400> 209
Met Lys Lys Arg Lys Val Leu Ile Pro Leu Met Ala Leu Ser Thr Ile
1 5 10 15
Leu Val Ser Ser Thr Gly Asn Leu Glu Val Ile Gln Ala Glu Val Lys
20 25 30
Gln Glu Asn Arg Leu Leu Asn Glu Ser Glu Ser Ser Ser Gln Gly Leu
35 40 45
Leu Gly Tyr Tyr Phe Ser Asp Leu Asn Phe Gln Ala Pro Met Val Val
50 55 60
Thr Ser Ser Thr Thr Gly Asp Leu Ser Ile Pro Ser Ser Glu Leu Glu
65 70 75 80
Asn Ile Pro Ser Glu Asn Gln Tyr Phe Gln Ser Ala Ile Trp Ser Gly
85 90 95
Phe Ile Lys Val Lys Lys Ser Asp Glu Tyr Thr Phe Ala Thr Ser Ala
100 105 110
Asp Asn His Val Thr Met Trp Val Asp Asp Gln Glu Val Ile Asn Lys
115 120 125
Ala Ser Asn Ser Asn Lys Ile Arg Leu Glu Lys Gly Arg Leu Tyr Gln
130 135 140
Ile Lys Ile Gln Tyr Gln Arg Glu Asn Pro Thr Glu Lys Gly Leu Asp
145 150 155 160
Phe Lys Leu Tyr Trp Thr Asp Ser Gln Asn Lys Lys Glu Val Ile Ser
165 170 175
Ser Asp Asn Leu Gln Leu Pro Glu Leu Lys Gln Lys Ser Ser Asn Ser
180 185 190
Arg Lys Lys Arg Ser Thr Ser Ala Gly Pro Thr Val Pro Asp Arg Asp
195 200 205
Asn Asp Gly Ile Pro Asp Ser Leu Glu Val Glu Gly Tyr Thr Val Asp
210 215 220
Val Lys Asn Lys Arg Thr Phe Leu Ser Pro Trp Ile Ser Asn Ile His
225 230 235 240
Glu Lys Lys Gly Leu Thr Lys Tyr Lys Ser Ser Pro Glu Lys Trp Ser
245 250 255
Thr Ala Ser Asp Pro Tyr Ser Asp Phe Glu Lys Val Thr Gly Arg Ile
260 265 270
Asp Lys Asn Val Ser Pro Glu Ala Arg His Pro Leu Val Ala Ala Tyr
275 280 285

```
Pro Ile Val His Val Asp Met Glu Asn Ile Ile Leu Ser Lys Asn Glu
    290                 295                 300
Asp Gln Ser Thr Gln Asn Thr Asp Ser Gln Thr Arg Thr Ile Ser Lys
305                 310                 315                 320
Asn Thr Ser Thr Ser Arg Thr His Thr Ser Glu Val His Gly Asn Ala
                325                 330                 335
Glu Val His Ala Ser Phe Phe Asp Ile Gly Gly Ser Val Ser Ala Gly
            340                 345                 350
Phe Ser Asn Ser Asn Ser Ser Thr Val Ala Ile Asp His Ser Leu Ser
        355                 360                 365
Leu Ala Gly Glu Arg Thr Trp Ala Glu Thr Met Gly Leu Asn Thr Ala
    370                 375                 380
Asp Thr Ala Arg Leu Asn Ala Asn Ile Arg Tyr Val Asn Thr Gly Thr
385                 390                 395                 400
Ala Pro Ile Tyr Asn Val Leu Pro Thr Thr Ser Leu Val Leu Gly Lys
                405                 410                 415
Asn Gln Thr Leu Ala Thr Ile Lys Ala Lys Glu Asn Gln Leu Ser Gln
            420                 425                 430
Ile Leu Ala Pro Asn Asn Tyr Tyr Pro Ser Lys Asn Leu Ala Pro Ile
        435                 440                 445
Ala Leu Asn Ala Gln Asp Asp Phe Ser Ser Thr Pro Ile Thr Met Asn
    450                 455                 460
Tyr Asn Gln Phe Leu Glu Leu Glu Lys Thr Lys Gln Leu Arg Leu Asp
465                 470                 475                 480
Thr Asp Gln Val Tyr Gly Asn Ile Ala Thr Tyr Asn Phe Glu Asn Gly
                485                 490                 495
Arg Val Arg Val Asp Thr Gly Ser Asn Trp Ser Glu Val Leu Pro Gln
            500                 505                 510
Ile Gln Glu Thr Thr Ala Arg Ile Ile Phe Asn Gly Lys Asp Leu Asn
        515                 520                 525
Leu Val Glu Arg Arg Ile Ala Ala Val Asn Pro Ser Asp Pro Leu Glu
    530                 535                 540
Thr Thr Lys Pro Asp Met Thr Leu Lys Glu Ala Leu Lys Ile Ala Phe
545                 550                 555                 560
Gly Phe Asn Glu Pro Asn Gly Asn Leu Gln Tyr Gln Gly Lys Asp Ile
                565                 570                 575
Thr Glu Phe Asp Phe Asn Phe Asp Gln Gln Thr Ser Gln Asn Ile Lys
            580                 585                 590
Asn Gln Leu Ala Glu Leu Asn Ala Thr Asn Ile Tyr Thr Val Leu Asp
        595                 600                 605
Lys Ile Lys Leu Asn Ala Lys Met Asn Ile Leu Ile Arg Asp Lys Arg
    610                 615                 620
Phe His Tyr Asp Arg Asn Asn Ile Ala Val Gly Ala Asp Glu Ser Val
625                 630                 635                 640
Val Lys Glu Ala His Arg Glu Val Ile Asn Ser Ser Thr Glu Gly Leu
                645                 650                 655
Leu Leu Asn Ile Asp Lys Asp Ile Arg Lys Ile Leu Ser Gly Tyr Ile
            660                 665                 670
Val Glu Ile Glu Asp Thr Glu Gly Leu Lys Glu Val Ile Asn Asp Arg
        675                 680                 685
Tyr Asp Met Leu Asn Ile Ser Ser Leu Arg Gln Asp Gly Lys Thr Phe
    690                 695                 700
Ile Asp Phe Lys Lys Tyr Asn Asp Lys Leu Pro Leu Tyr Ile Ser Asn
705                 710                 715                 720
Pro Asn Tyr Lys Val Asn Val Tyr Ala Val Thr Lys Glu Asn Thr Ile
                725                 730                 735
Ile Asn Pro Ser Glu Asn Gly Asp Thr Ser Thr Asn Gly Ile Lys Lys
            740                 745                 750
Ile Leu Ile Phe Ser Lys Lys Gly Tyr Glu Ile Gly
        755                 760
```

<210> 210
<211> 588
<212> PRT
<213> Ebola virus

<220>
<221> VARIANT
<222> 120
<223> Xaa = Any Amino Acid

<400> 210
His Gly Phe Arg Phe Glu Val Lys Lys Arg Asp Gly Val Lys Arg Leu
1 5 10 15
Glu Glu Leu Leu Pro Ala Val Ser Ser Gly Lys Asn Ile Lys Arg Thr
20 25 30
Leu Ala Ala Met Pro Glu Glu Glu Thr Thr Glu Ala Asn Ala Gly Gln
35 40 45
Phe Leu Ser Phe Ala Ser Leu Phe Leu Pro Lys Leu Val Val Gly Glu
50 55 60
Lys Ala Cys Leu Glu Lys Val Gln Arg Gln Ile Gln Val His Ala Glu
65 70 75 80
Gln Gly Leu Ile Gln Tyr Pro Thr Ala Trp Gln Ser Val Gly His Met
85 90 95
Met Val Ile Phe Arg Leu Met Arg Thr Asn Phe Leu Ile Lys Phe Leu
100 105 110
Leu Ile His Gln Gly Met His Xaa Val Ala Gly His Asp Ala Asn Asp
115 120 125
Ala Val Ile Ser Asn Ser Val Ala Gln Ala Arg Phe Ser Gly Leu Leu
130 135 140
Ile Val Lys Thr Val Leu Asp His Ile Leu Gln Lys Thr Glu Arg Gly
145 150 155 160
Val Arg Leu His Pro Leu Ala Arg Thr Ala Lys Val Lys Asn Glu Val
165 170 175
Asn Ser Phe Lys Ala Ala Leu Ser Ser Leu Ala Lys His Gly Glu Tyr
180 185 190
Ala Pro Phe Ala Arg Leu Leu Asn Leu Ser Gly Val Asn Asn Leu Glu
195 200 205
His Gly Leu Phe Pro Gln Leu Ser Ala Ile Ala Leu Gly Val Ala Thr
210 215 220
Ala His Gly Ser Thr Leu Ala Gly Val Asn Val Gly Glu Gln Tyr Gln
225 230 235 240
Gln Leu Arg Glu Ala Ala Thr Glu Ala Glu Lys Gln Leu Gln Gln Tyr
245 250 255
Ala Glu Ser Arg Glu Leu Asp His Leu Gly Leu Asp Asp Gln Glu Lys
260 265 270
Lys Ile Leu Met Asn Phe His Gln Lys Lys Asn Glu Ile Ser Phe Gln
275 280 285
Gln Thr Asn Ala Met Val Thr Leu Arg Lys Glu Arg Leu Ala Lys Leu
290 295 300
Thr Glu Ala Ile Thr Ala Ala Ser Leu Pro Lys Thr Ser Gly His Tyr
305 310 315 320
Asp Asp Asp Asp Asp Ile Pro Phe Pro Gly Pro Ile Asn Asp Asp Asp
325 330 335
Asn Pro Gly His Gln Asp Asp Asp Pro Thr Asp Ser Gln Asp Thr Thr
340 345 350
Ile Pro Asp Val Val Val Asp Pro Asp Asp Gly Ser Tyr Gly Glu Tyr
355 360 365
Gln Ser Tyr Ser Glu Asn Gly Met Asn Ala Pro Asp Asp Leu Val Leu
370 375 380

```
Phe Asp Leu Asp Glu Asp Asp Glu Asp Thr Lys Pro Val Pro Asn Arg
385                 390                 395                 400
Ser Thr Lys Gly Gly Gln Gln Lys Asn Ser Gln Lys Gly Gln His Thr
                405                 410                 415
Glu Gly Arg Gln Thr Gln Ser Arg Pro Thr Gln Asn Val Pro Gly Pro
            420                 425                 430
His Arg Thr Ile His His Ala Ser Ala Pro Leu Thr Asp Asn Asp Arg
        435                 440                 445
Arg Asn Glu Pro Ser Gly Ser Thr Ser Pro Arg Met Leu Thr Pro Ile
    450                 455                 460
Asn Glu Glu Ala Asp Pro Leu Asp Asp Ala Asp Asp Glu Thr Ser Ser
465                 470                 475                 480
Leu Pro Pro Leu Glu Ser Asp Asp Glu Glu Gln Asp Arg Gly Gly Thr
                485                 490                 495
Ser Asn Arg Thr Pro Thr Val Ala Pro Pro Ala Pro Val Tyr Arg Asp
            500                 505                 510
His Ser Glu Lys Lys Glu Leu Pro Gln Asp Glu Arg Gln Asp Gln Asp
        515                 520                 525
His Thr Gln Glu Ala Arg Asn Gln Asp Ser Asp Asn Thr Gln Pro Glu
    530                 535                 540
His Ser Phe Glu Glu Met Tyr Arg His Ile Leu Arg Ser Gln Gly Pro
545                 550                 555                 560
Phe Asp Ala Val Leu Tyr Tyr His Met Met Lys Asp Glu Pro Val Val
                565                 570                 575
Phe Ser Thr Ser Asp Gly Lys Glu Tyr Thr Tyr Pro
            580                 585
```

<210> 211
<211> 2280
<212> PRT
<213> Hepatitis C Virus

<400> 211

```
Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Tyr
 1                5                  10                  15
Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
            20                  25                  30
Gly Val Tyr Val Leu Pro Arg Arg Gly Pro Thr Leu Gly Val Arg Ala
        35                  40                  45
Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
    50                  55                  60
Ile Pro Lys Ala Arg Arg Pro Glu Gly Arg Ala Trp Ala Gln Pro Gly
65                  70                  75                  80
Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Leu Gly Trp Ala Gly Trp
                85                  90                  95
Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Thr Asp Pro
            100                 105                 110
Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys
        115                 120                 125
Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Leu
    130                 135                 140
Gly Gly Ala Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp
145                 150                 155                 160

Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile
                165                 170                 175
Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Ile Pro Ala Ser Ala Tyr
            180                 185                 190
Gln Val Arg Asn Ala Ser Gly Leu Tyr His Val Thr Asn Asp Cys Ser
        195                 200                 205
```

```
Asn Ser Ser Ile Val Tyr Glu Ala Ala Gly Met Ile Met His Thr Pro
    210                 215                 220
Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ala Ser Arg Cys Trp Val
225                 230                 235                 240
Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Thr Ser Ile Pro Thr Thr
                245                 250                 255
Thr Ile Arg Arg His Val Asp Leu Leu Val Gly Ala Ala Ala Phe Cys
            260                 265                 270
Ser Ala Met Tyr Val Gly Asp Leu Cys Gly Ser Val Phe Leu Val Ser
        275                 280                 285
Gln Leu Phe Thr Phe Ser Pro Arg Arg Tyr Glu Thr Val Gln Asp Cys
    290                 295                 300
Asn Cys Ser Ile Tyr Pro Gly His Val Ser Gly His Arg Met Ala Trp
305                 310                 315                 320
Asp Met Met Met Asn Trp Ser Pro Thr Thr Ala Leu Val Val Ser Gln
                325                 330                 335
Leu Leu Arg Ile Pro Gln Ala Val Val Asp Met Val Ala Gly Ala His
            340                 345                 350
Trp Gly Val Leu Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly Asn Trp
        355                 360                 365
Ala Lys Val Leu Ile Val Met Leu Leu Phe Ala Gly Val Asp Gly Val
    370                 375                 380
Thr Tyr Thr Thr Gly Gly Ser Gln Ala Arg His Thr Gln Ser Val Thr
385                 390                 395                 400
Ser Phe Phe Thr Gln Gly Pro Ala Gln Arg Ile Gln Leu Ile Asn Thr
                405                 410                 415
Asn Gly Ser Trp His Ile Asn Arg Thr Ala Leu Asn Cys Asn Glu Ser
            420                 425                 430
Leu Asn Thr Gly Phe Phe Ala Ala Leu Phe Tyr Ala His Lys Phe Asn
        435                 440                 445
Ser Ser Gly Cys Pro Glu Arg Met Ala Ser Cys Ser Ser Ile Asp Lys
    450                 455                 460
Phe Ala Gln Gly Trp Gly Pro Ile Thr Tyr Thr Glu Pro Arg Asp Leu
465                 470                 475                 480
Asp Gln Arg Pro Tyr Cys Trp His Tyr Ala Pro Arg Gln Cys Gly Ile
                485                 490                 495
Val Pro Ala Ser Gln Val Cys Gly Pro Val Tyr Cys Phe Thr Pro Ser
            500                 505                 510
Pro Val Val Val Gly Thr Thr Asp Arg Ser Gly Ala Pro Thr Tyr Asn
        515                 520                 525
Trp Gly Ala Asn Glu Thr Asp Val Leu Leu Leu Asn Asn Thr Arg Pro
    530                 535                 540
Pro Gln Gly Asn Trp Phe Gly Cys Thr Trp Met Asn Ser Thr Gly Phe
545                 550                 555                 560
Thr Lys Thr Cys Gly Gly Pro Pro Cys Asn Ile Gly Gly Val Gly Asn
                565                 570                 575
Leu Thr Leu Thr Cys Pro Thr Asp Cys Phe Arg Lys His Pro Glu Ala
            580                 585                 590
Thr Tyr Thr Lys Cys Gly Ser Gly Pro Trp Leu Thr Pro Arg Cys Ile
        595                 600                 605
Val Asp Tyr Pro Tyr Arg Leu Trp His Tyr Pro Cys Thr Val Asn Phe
    610                 615                 620
Thr Ile Phe Lys Val Arg Met Tyr Val Gly Gly Val Glu His Arg Leu
625                 630                 635                 640
Ser Ala Ala Cys Asn Trp Thr Arg Gly Glu Arg Cys Asp Leu Glu Asp
                645                 650                 655
Arg Asp Arg Ser Glu Leu Ser Pro Leu Leu Leu Ser Thr Thr Glu Trp
            660                 665                 670
Gln Thr Leu Pro Cys Ser Phe Thr Thr Leu Pro Ala Leu Ser Thr Gly
        675                 680                 685
```

```
Leu Ile His Leu His Gln Asn Ile Val Asp Val Gln Tyr Leu Tyr Gly
    690                 695                 700
Ile Gly Ser Ala Val Val Ser Phe Val Ile Lys Trp Glu Tyr Ile Val
705                 710                 715                 720
Leu Leu Phe Leu Leu Leu Ala Asp Ala Arg Val Cys Ala Cys Leu Trp
                725                 730                 735
Met Met Leu Leu Ile Ala Gln Ala Glu Ala Ala Leu Glu Asn Leu Val
            740                 745                 750
Val Leu Asn Ala Ala Ser Leu Ala Gly Ala Asp Gly Ile Leu Ser Phe
        755                 760                 765
Leu Val Phe Phe Cys Ala Ala Trp Tyr Ile Lys Gly Arg Leu Val Pro
    770                 775                 780
Gly Ala Ala Tyr Ala Leu Tyr Gly Val Trp Pro Leu Leu Leu Leu Leu
785                 790                 795                 800
Leu Ala Leu Pro Pro Arg Ala Tyr Ala Met Asp Arg Glu Met Ala Ala
                805                 810                 815
Ser Cys Gly Gly Val Val Phe Val Gly Leu Ile Leu Leu Thr Leu Ser
            820                 825                 830
Pro His Tyr Lys Val Phe Leu Ala Arg Leu Ile Trp Trp Leu Gln Tyr
        835                 840                 845
Phe Ile Thr Arg Ala Glu Ala His Leu Cys Val Trp Val Pro Pro Leu
    850                 855                 860
Asn Val Arg Gly Gly Arg Asp Ala Ile Ile Leu Leu Thr Cys Ala Ala
865                 870                 875                 880
His Pro Glu Leu Ile Phe Asp Ile Thr Lys Leu Leu Leu Ala Ile Leu
                885                 890                 895
Gly Pro Leu Met Val Leu Gln Ala Ala Ile Thr Ala Met Pro Tyr Phe
            900                 905                 910
Val Arg Ala Gln Gly Leu Ile Arg Ala Cys Met Leu Val Arg Lys Val
        915                 920                 925
Ala Gly Gly His Tyr Val Gln Met Ala Phe Met Lys Leu Ala Ala Leu
    930                 935                 940
Thr Gly Thr Tyr Val Tyr Asp His Leu Thr Pro Leu Gln Asp Trp Ala
945                 950                 955                 960
His Ala Gly Leu Arg Asp Leu Ala Val Ala Val Glu Pro Val Val Phe
                965                 970                 975
Ser Asp Met Glu Thr Lys Ile Ile Thr Trp Gly Ala Asp Thr Ala Ala
            980                 985                 990
Cys Gly Asp Ile Ile Leu Gly Leu Pro Val Ser Ala Arg Arg Gly Arg
        995                 1000                1005
Glu Ile Leu Leu Gly Pro Ala Asp Ser Ile Glu Gly Gln Gly Trp Arg
    1010                1015                1020
Leu Leu Ala Pro Ile Thr Ala Tyr Ala Gln Gln Thr Arg Gly Leu Leu
1025                1030                1035                1040
Gly Cys Ile Val Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu
                1045                1050                1055
Gly Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr
            1060                1065                1070
Cys Val Asn Gly Val Cys Trp Thr Val Phe His Gly Ala Gly Ser Lys
        1075                1080                1085
Thr Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val
    1090                1095                1100
Asp Gln Asp Leu Val Gly Trp His Ala Pro Pro Gly Ala Arg Ser Leu
1105                1110                1115                1120
Thr Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His
                1125                1130                1135
Ala Asp Val Ile Pro Val Arg Arg Arg Gly Asp Gly Arg Gly Ser Leu
            1140                1145                1150
Leu Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro
        1155                1160                1165
Leu Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val
```

1170 1175 1180
Cys Thr Arg Gly Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser
1185 1190 1195 1200
Met Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro
1205 1210 1215
Pro Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr
1220 1225 1230
Gly Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly
1235 1240 1245
Tyr Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe
1250 1255 1260
Gly Ala Tyr Met Ser Lys Ala His Gly Thr Asp Pro Asn Ile Arg Thr
1265 1270 1275 1280
Gly Val Arg Thr Ile Thr Thr Gly Ala Pro Ile Thr Tyr Ser Thr Tyr
1285 1290 1295
Gly Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile
1300 1305 1310
Ile Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly
1315 1320 1325
Ile Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val
1330 1335 1340
Val Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro
1345 1350 1355 1360
Asn Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr
1365 1370 1375
Gly Lys Ala Ile Pro Leu Glu Ala Ile Lys Gly Gly Arg His Leu Ile
1380 1385 1390
Phe Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser
1395 1400 1405
Gly Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser
1410 1415 1420
Val Ile Pro Thr Ser Gly Asp Val Val Ile Val Ala Thr Asp Ala Leu
1425 1430 1435 1440
Met Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr
1445 1450 1455
Cys Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile
1460 1465 1470
Glu Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg
1475 1480 1485
Gly Arg Thr Gly Arg Gly Arg Gly Gly Ile Tyr Arg Phe Val Thr Pro
1490 1495 1500
Gly Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys
1505 1510 1515 1520
Tyr Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr
1525 1530 1535
Val Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln
1540 1545 1550
Asp His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile
1555 1560 1565
Asp Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro
1570 1575 1580
Tyr Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro
1585 1590 1595 1600
Pro Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro
1605 1610 1615
Thr Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln
1620 1625 1630
Asn Glu Ile Thr Leu Thr His Pro Ile Thr Lys Phe Ile Met Ala Cys
1635 1640 1645
Met Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly
1650 1655 1660

Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val
1665 1670 1675 1680
Val Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Val Val Pro
1685 1690 1695
Asp Arg Glu Val Leu Tyr Arg Glu Phe Asp Glu Met Glu Glu Cys Ala
1700 1705 1710
Ser His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe
1715 1720 1725
Lys Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu
1730 1735 1740
Ala Ala Ala Pro Val Val Glu Ser Arg Trp Arg Ala Leu Glu Ala Phe
1745 1750 1755 1760
Trp Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala
1765 1770 1775
Gly Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala
1780 1785 1790
Phe Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Asn Thr Leu Leu
1795 1800 1805
Phe Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser
1810 1815 1820
Ala Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Ile Gly
1825 1830 1835 1840
Ser Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly
1845 1850 1855
Ala Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu
1860 1865 1870
Ala Pro Ser Ala Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser
1875 1880 1885
Pro Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg
1890 1895 1900
His Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile
1905 1910 1915 1920
Ala Phe Ala Ser Arg Gly Asn His Val Ser Pro Thr His Tyr Val Pro
1925 1930 1935
Glu Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr
1940 1945 1950
Ile Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys
1955 1960 1965
Ser Thr Pro Cys Ser Gly Ser Trp Leu Lys Asp Val Trp Asp Trp Ile
1970 1975 1980
Cys Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu
1985 1990 1995 2000
Pro Lys Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys
2005 2010 2015
Gly Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly
2020 2025 2030
Ala Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly
2035 2040 2045
Pro Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala
2050 2055 2060
Tyr Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg
2065 2070 2075 2080
Ala Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Ile Thr Arg Val
2085 2090 2095
Gly Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys
2100 2105 2110
Pro Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Leu Asp Gly Val
2115 2120 2125
Arg Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Asp
2130 2135 2140
Val Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu

2145 2150 2155 2160
Pro Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr
2165 2170 2175
Asp Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg
2180 2185 2190
Gly Ser Pro Pro Ser Leu Ala Ser Ser Ser Ala Ser Gln Leu Ser Ala
2195 2200 2205
Pro Ser Leu Lys Ala Thr Cys Thr Thr His His Asp Ser Pro Asp Ala
2210 2215 2220
Asp Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Asn
2225 2230 2235 2240
Ile Thr Arg Val Glu Ser Glu Asn Lys Val Val Ile Leu Asp Ser Phe
2245 2250 2255
Asp Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Ala Ala
2260 2265 2270
Glu Ile Leu Arg Lys Ser Lys Lys
2275 2280

<210> 212
<211> 128
<212> PRT
<213> Homo sapiens

<400> 212
Met Arg Thr Leu Asp Leu Ile Asp Glu Ala Tyr Gly Leu Asp Phe Tyr
1 5 10 15
Ile Leu Lys Thr Pro Lys Glu Asp Leu Cys Ser Lys Phe Gly Met Glu
20 25 30
Leu Lys Arg Gly Met Leu Leu Arg Leu Ala Arg Gln Asp Pro Gln Leu
35 40 45
His Pro Glu Asp Pro Glu Arg Arg Ala Ala Ile Tyr Asp Lys Tyr Lys
50 55 60
Glu Phe Ala Ile Pro Glu Glu Glu Ala Glu Trp Val Gly Leu Thr Leu
65 70 75 80
Glu Glu Ala Ile Glu Lys Gln Arg Leu Leu Glu Glu Lys Asp Pro Val
85 90 95
Pro Leu Phe Lys Ile Tyr Val Ala Glu Leu Ile Gln Gln Leu Gln Gln
100 105 110
Gln Ala Leu Ser Glu Pro Ala Val Val Gln Lys Thr Ala Ser Gly Gln
115 120 125

<210> 213
<211> 1255
<212> PRT
<213> Homo sapiens

<400> 213
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95

```
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335
Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
            340                 345                 350
Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
        355                 360                 365
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
    370                 375                 380
Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
                405                 410                 415
Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
            420                 425                 430
Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
        435                 440                 445
Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
    450                 455                 460
Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480
Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
                485                 490                 495
Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
            500                 505                 510
Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
        515                 520                 525
Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
    530                 535                 540
Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560
Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
                565                 570                 575
Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
```

```
            580                 585                 590
Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
        595                 600                 605
Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
    610                 615                 620
Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640
Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
                645                 650                 655
Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
            660                 665                 670
Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
        675                 680                 685
Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
    690                 695                 700
Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705                 710                 715                 720
Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
                725                 730                 735
Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
            740                 745                 750
Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
        755                 760                 765
Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
    770                 775                 780
Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785                 790                 795                 800
Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
                805                 810                 815
Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
            820                 825                 830
Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
        835                 840                 845
Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
    850                 855                 860
Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880
Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
                885                 890                 895
Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
            900                 905                 910
Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
        915                 920                 925
Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
    930                 935                 940
Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960
Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
                965                 970                 975
Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
            980                 985                 990
Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
        995                 1000                1005
Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
    1010                1015                1020
Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
1025                1030                1035                1040
Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
                1045                1050                1055
Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg
            1060                1065                1070
```

```
Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
        1075                1080                1085
Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
    1090                1095                1100
Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
1105                1110                1115                1120
Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
                1125                1130                1135
Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
            1140                1145                1150
Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
        1155                1160                1165
Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
    1170                1175                1180
Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
1185                1190                1195                1200
Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
                1205                1210                1215
Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
            1220                1225                1230
Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
        1235                1240                1245
Leu Gly Leu Asp Val Pro Val
    1250                1255
```

<210> 214
<211> 574
<212> PRT
<213> Respiratory Syncytial Virus

<400> 214

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
 1                5                  10                  15
Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30
Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45
Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60
Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80
Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Pro Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110
Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125
Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140
Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys Val Leu His Leu
145                 150                 155                 160
Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175
Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
            180                 185                 190
Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
        195                 200                 205
Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220
```

```
Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240
Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255
Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270
Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285
Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300
Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320
Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335
Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350
Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365
Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Ile Asn Leu Cys Asn Val
    370                 375                 380
Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400
Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415
Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430
Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Met Asp

        435                 440                 445
Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460
Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480
Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495
Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510
Leu His Asn Val Asn Ala Gly Lys Ser Thr Thr Asn Ile Met Ile Thr
        515                 520                 525
Thr Ile Ile Ile Val Ile Ile Val Ile Leu Leu Ser Leu Ile Ala Val
    530                 535                 540
Gly Leu Leu Leu Tyr Cys Lys Ala Arg Ser Thr Pro Val Thr Leu Ser
545                 550                 555                 560
Lys Asp Gln Leu Ser Gly Ile Asn Asn Ile Ala Phe Ser Asn
                565                 570
```

<210> 215
<211> 151
<212> PRT
<213> Human Immunodeficiency Virus 2

<400> 215

```
Asp Val Val Lys Arg Gln Gln Glu Leu Leu Arg Leu Thr Val Trp Gly
 1               5                  10                  15
Thr Lys Asn Leu Gln Ala Arg Val Thr Ala Ile Glu Lys Tyr Leu Lys
            20                  25                  30
Asp Gln Ala His Val Asn Ser Trp Gly Cys Ala Phe Arg Gln Val Cys
        35                  40                  45
His Thr Thr Val Pro Trp Val Asn Asp Thr Leu Thr Pro Asp Trp Asp
    50                  55                  60
```

```
Asn Met Thr Trp Gln Glu Trp Glu Glu Lys Val Arg Tyr Leu Glu Ala
65                  70                  75                  80
Asn Ile Ser Gln Ser Leu Glu Gln Ala Gln Ile Leu Gln Glu Lys Asn
                85                  90                  95
Met Tyr Glu Leu Gln Lys Leu Asn Ser Trp Asp Ile Phe Gly Asn Trp
            100                 105                 110
Phe Asp Leu Thr Ser Trp Val Lys Tyr Ile Gln Tyr Gly Val Cys Ile
        115                 120                 125
Ile Val Gly Ile Val Ala Leu Arg Ile Val Ile Tyr Val Val Gln Met
    130                 135                 140
Leu Ser Arg Leu Arg Lys Gly
145                 150
```

<210> 216
<211> 522
<212> PRT
<213> Human Immunodeficiency Virus

<400> 216

```
Met Gly Ala Arg Asn Ser Val Leu Arg Gly Lys Lys Ala Asp Glu Leu
 1                  5                  10                  15
Glu Arg Ile Arg Leu Arg Pro Gly Gly Lys Lys Lys Tyr Arg Leu Lys
            20                  25                  30
His Ile Val Trp Ala Ala Asn Lys Leu Asp Arg Phe Gly Leu Ala Glu
        35                  40                  45
Ser Leu Leu Glu Ser Lys Glu Gly Cys Gln Lys Ile Leu Thr Val Leu
    50                  55                  60
Asp Pro Met Val Pro Thr Gly Ser Glu Asn Leu Lys Ser Leu Phe Asn
65                  70                  75                  80
Thr Val Cys Val Ile Trp Cys Ile His Ala Glu Glu Lys Val Lys Asp
                85                  90                  95
Thr Glu Gly Ala Lys Gln Ile Val Arg Arg His Leu Val Ala Glu Thr
            100                 105                 110
Gly Thr Ala Glu Lys Met Pro Ser Thr Ser Arg Pro Thr Ala Pro Ser
        115                 120                 125
Ser Glu Lys Gly Gly Asn Tyr Pro Val Gln His Val Gly Gly Asn Tyr
    130                 135                 140
Thr His Ile Pro Leu Ser Pro Arg Thr Leu Asn Ala Trp Val Lys Leu
145                 150                 155                 160
Val Glu Glu Lys Lys Phe Gly Ala Glu Val Val Pro Gly Phe Gln Ala
                165                 170                 175
Leu Ser Glu Gly Cys Thr Pro Tyr Asp Ile Asn Gln Met Leu Asn Cys
            180                 185                 190
Val Gly Asp His Gln Ala Ala Met Gln Ile Ile Arg Glu Ile Ile Asn
        195                 200                 205
Glu Glu Ala Ala Glu Trp Asp Val Gln His Pro Ile Pro Gly Pro Leu
    210                 215                 220
Pro Ala Gly Gln Leu Arg Glu Pro Arg Gly Ser Asp Ile Ala Gly Thr
225                 230                 235                 240
Thr Ser Thr Val Glu Glu Gln Ile Gln Trp Met Phe Arg Pro Gln Asn
                245                 250                 255
Pro Val Pro Val Gly Asn Ile Tyr Arg Arg Trp Ile Gln Ile Gly Leu
            260                 265                 270
Gln Lys Cys Val Arg Met Tyr Asn Pro Thr Asn Ile Leu Asp Ile Lys
        275                 280                 285
Gln Gly Pro Lys Glu Pro Phe Gln Ser Tyr Val Asp Arg Phe Tyr Lys
    290                 295                 300
Ser Leu Arg Ala Glu Gln Thr Asp Pro Ala Val Lys Asn Trp Met Thr
305                 310                 315                 320
Gln Thr Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Leu Val Leu
```

```
                325                 330                 335
Lys Gly Leu Gly Met Asn Pro Thr Leu Glu Glu Met Leu Thr Ala Cys
            340                 345                 350
Gln Gly Val Gly Gly Pro Gly Gln Lys Ala Arg Leu Met Ala Glu Ala
        355                 360                 365
Leu Lys Glu Val Ile Gly Pro Ala Pro Ile Pro Phe Ala Ala Ala Gln
    370                 375                 380
Gln Arg Lys Ala Phe Lys Cys Trp Asn Cys Gly Lys Glu Gly His Ser
385                 390                 395                 400
Ala Arg Gln Cys Arg Ala Pro Arg Arg Gln Gly Cys Trp Lys Cys Gly
                405                 410                 415
Lys Pro Gly His Ile Met Thr Asn Cys Pro Asp Arg Gln Ala Gly Phe
            420                 425                 430
Leu Gly Leu Gly Pro Trp Gly Lys Lys Pro Arg Asn Phe Pro Val Ala
        435                 440                 445
Gln Val Pro Gln Gly Leu Thr Pro Thr Ala Pro Pro Val Asp Pro Ala
    450                 455                 460
Val Asp Leu Leu Glu Lys Tyr Met Gln Gln Gly Lys Arg Gln Arg Glu
465                 470                 475                 480
Gln Arg Glu Arg Pro Tyr Lys Glu Val Thr Glu Asp Leu Leu His Leu
                485                 490                 495
Glu Gln Gly Glu Thr Pro Tyr Arg Glu Pro Pro Thr Glu Asp Leu Leu
            500                 505                 510
His Leu Asn Ser Leu Phe Gly Lys Asp Gln
        515                 520
```

<210> 217
<211> 860
<212> PRT
<213> Human Immunodeficiency Virus 2

<400> 217

```
Met Glu Pro Gly Arg Asn Gln Leu Phe Val Val Ile Leu Leu Thr Ser
 1                5                  10                  15
Ala Cys Leu Val Tyr Cys Ser Gln Tyr Val Thr Val Phe Tyr Gly Ile
            20                  25                  30
Pro Ala Trp Lys Asn Ala Ser Ile Pro Leu Phe Cys Ala Thr Lys Asn
        35                  40                  45
Arg Asp Thr Trp Gly Thr Ile Gln Cys Leu Pro Asp Asn Asp Asp Tyr
    50                  55                  60
Gln Glu Ile Ile Leu Asn Val Thr Glu Ala Phe Asp Ala Trp Asn Asn
65                  70                  75                  80
Thr Val Thr Glu Gln Ala Val Glu Asp Val Trp His Leu Phe Glu Thr
                85                  90                  95
Ser Ile Lys Pro Cys Val Lys Leu Thr Pro Leu Cys Val Ala Met Asn
            100                 105                 110
Cys Ser Arg Val Gln Gly Asn Thr Thr Thr Pro Asn Pro Arg Thr Ser
        115                 120                 125
Ser Ser Thr Thr Ser Arg Pro Pro Thr Ser Ala Ala Ser Ile Ile Asn
    130                 135                 140
Glu Thr Ser Asn Cys Ile Glu Asn Asn Thr Cys Ala Gly Leu Gly Tyr
145                 150                 155                 160
Glu Glu Met Met Gln Cys Glu Phe Asn Met Lys Gly Leu Glu Gln Asp
                165                 170                 175
Lys Lys Arg Arg Tyr Lys Asp Thr Trp Tyr Leu Glu Asp Val Val Cys
            180                 185                 190
Asp Asn Thr Thr Ala Gly Thr Cys Tyr Met Arg His Cys Asn Thr Ser
        195                 200                 205
Ile Ile Lys Glu Ser Cys Asp Lys His Tyr Trp Asp Ala Met Arg Phe
    210                 215                 220
```

```
Arg Tyr Cys Ala Pro Pro Gly Phe Ala Leu Leu Arg Cys Asn Asp Thr
225                 230                 235                 240
Asn Tyr Ser Gly Phe Glu Pro Lys Cys Thr Lys Val Val Ala Ala Ser
                245                 250                 255
Cys Thr Arg Met Met Glu Thr Gln Thr Ser Thr Trp Phe Gly Phe Asn
            260                 265                 270
Gly Thr Arg Ala Glu Asn Arg Thr Tyr Ile Tyr Trp His Gly Arg Asp
        275                 280                 285
Asn Arg Thr Ile Ile Ser Leu Asn Lys Tyr Tyr Asn Leu Thr Met Arg
    290                 295                 300
Cys Lys Arg Pro Gly Asn Lys Thr Val Leu Pro Ile Thr Leu Met Ser
305                 310                 315                 320
Gly Leu Val Phe His Ser Gln Pro Ile Asn Thr Arg Pro Arg Gln Ala
                325                 330                 335
Trp Cys Arg Phe Gly Gly Arg Trp Arg Glu Ala Met Gln Glu Val Lys
            340                 345                 350
Gln Thr Leu Val Gln His Pro Arg Tyr Lys Gly Ile Asn Asp Thr Gly
        355                 360                 365
Lys Ile Asn Phe Thr Lys Pro Gly Ala Gly Ser Asp Pro Glu Val Ala
    370                 375                 380
Phe Met Trp Thr Asn Cys Arg Gly Glu Phe Leu Tyr Cys Asn Met Thr
385                 390                 395                 400
Trp Phe Leu Asn Trp Val Glu Asp Lys Asn Gln Thr Arg Arg Asn Tyr
                405                 410                 415
Cys His Ile Lys Gln Ile Ile Asn Thr Trp His Lys Val Gly Lys Asn
            420                 425                 430
Val Tyr Leu Pro Pro Arg Glu Gly Glu Leu Ala Cys Glu Ser Thr Val
        435                 440                 445
Thr Ser Ile Ile Ala Asn Ile Asp Ile Asp Lys Asn Arg Thr His Thr
    450                 455                 460
Asn Ile Thr Phe Ser Ala Glu Val Ala Glu Leu Tyr Arg Leu Glu Leu
465                 470                 475                 480
Gly Asp Tyr Lys Leu Ile Glu Ile Thr Pro Ile Gly Phe Ala Pro Thr
                485                 490                 495
Asp Gln Arg Arg Tyr Ser Ser Thr Pro Val Arg Asn Lys Arg Gly Val
            500                 505                 510
Phe Val Leu Gly Phe Leu Gly Phe Leu Ala Thr Ala Gly Ser Ala Met
        515                 520                 525
Gly Ala Arg Ser Leu Thr Leu Ser Ala Gln Ser Arg Thr Leu Leu Ala
    530                 535                 540
Gly Ile Val Gln Gln Gln Gln Gln Leu Leu Asp Val Val Lys Arg Gln
545                 550                 555                 560
Gln Glu Met Leu Arg Leu Thr Val Trp Gly Thr Lys Asn Leu Gln Ala
                565                 570                 575
Arg Val Thr Ala Ile Glu Lys Tyr Leu Lys His Gln Ala Gln Leu Asn
            580                 585                 590
Ser Trp Gly Cys Ala Phe Arg Gln Val Cys His Thr Thr Val Pro Trp
        595                 600                 605
Val Asn Asp Ser Leu Ser Pro Asp Trp Lys Asn Met Thr Trp Gln Glu
    610                 615                 620
Trp Glu Lys Gln Val Arg Tyr Leu Glu Ala Asn Ile Ser Gln Ser Leu
625                 630                 635                 640
Glu Glu Ala Gln Ile Gln Gln Glu Lys Asn Met Tyr Glu Leu Gln Lys
                645                 650                 655
Leu Asn Ser Trp Asp Ile Leu Gly Asn Trp Phe Asp Leu Thr Ser Trp
            660                 665                 670
Val Lys Tyr Ile Gln Tyr Gly Val His Ile Val Val Gly Ile Ile Ala
        675                 680                 685
Leu Arg Ile Ala Ile Tyr Val Val Gln Leu Leu Ser Arg Phe Arg Lys
    690                 695                 700
Gly Tyr Arg Pro Val Phe Ser Ser Pro Pro Gly Tyr Leu Gln Gln Ile
```

```
705                 710                 715                 720
His Ile His Lys Asp Arg Gly Gln Pro Ala Asn Glu Gly Thr Glu Glu
                725                 730                 735
Asp Val Gly Gly Asp Ser Gly Tyr Asp Leu Trp Pro Trp Pro Ile Asn
            740                 745                 750
Tyr Val Gln Phe Leu Ile His Leu Leu Thr Arg Leu Leu Ile Gly Leu
        755                 760                 765
Tyr Asn Ile Cys Arg Asp Leu Leu Ser Lys Asn Ser Pro Thr Arg Arg
    770                 775                 780
Leu Ile Ser Gln Ser Leu Thr Ala Ile Arg Asp Trp Leu Arg Leu Lys
785                 790                 795                 800
Ala Ala Gln Leu Gln Tyr Gly Cys Glu Trp Ile Gln Glu Ala Phe Gln
                805                 810                 815
Ala Phe Ala Arg Thr Thr Arg Glu Thr Leu Ala Gly Ala Trp Gly Trp
            820                 825                 830
Leu Trp Glu Ala Ala Arg Arg Ile Gly Arg Gly Ile Leu Ala Val Pro
        835                 840                 845
Arg Arg Ile Arg Gln Gly Ala Glu Leu Ala Leu Leu
    850                 855                 860
```

<210> 218
<211> 25
<212> PRT
<213> Human Immunodeficiency Virus

<400> 218

```
Ser Glu Gly Asp Thr Asp Glu Leu Ala Lys Leu Val Glu Met Gly Asn
 1               5                  10                  15
Tyr Asp Leu Gly Asp Ala Ser Asp Leu
            20                  25
```

<210> 219
<211> 854
<212> PRT
<213> Human Immunodeficiency Virus

<400> 219

```
Met Arg Val Lys Gly Ile Met Arg Asn Cys Gln Gln Trp Trp Ile Trp
 1               5                  10                  15
Gly Ile Leu Gly Phe Trp Met Leu Leu Ile Cys Asn Gly Glu Gly Asn
            20                  25                  30
Leu Trp Val Thr Val Tyr Tyr Gly Val Pro Val Trp Lys Glu Ala Lys
        35                  40                  45
Thr Thr Leu Phe Cys Ala Ser Asp Ala Lys Gly Tyr Glu Arg Glu Val
    50                  55                  60
His Asn Ile Trp Ala Thr His Ala Cys Val Pro Thr Asp Pro Asn Pro
65                  70                  75                  80
Gln Glu Met Phe Leu His Asn Val Thr Glu Asn Phe Asn Met Trp Lys
                85                  90                  95
Asn Asp Met Val Asp Gln Met His Glu Asp Ile Ile Ser Leu Trp Asp
            100                 105                 110
Glu Ser Leu Lys Pro Cys Val Lys Leu Thr Pro Leu Cys Val Thr Leu
        115                 120                 125
Glu Cys Lys Asn Val Thr Thr Asn Val Thr Ile Asn Asn Ala Thr Ser
    130                 135                 140
Val Thr Ala Asn Asn Asn Thr Ser Asp Met Lys Asn Cys Ser Phe Asn
145                 150                 155                 160
Ala Thr Thr Glu Val Thr Asp Lys Ile Arg Lys Glu Asn Ala Leu Phe
                165                 170                 175
```

```
Tyr Thr Leu Asp Ile Val Pro Leu Asp Glu Asn Gln Asn Asn Ser Asn
            180                 185                 190
Tyr Arg Leu Ile Asn Cys Asn Thr Ser Lys Val Thr Gln Ala Cys Pro
        195                 200                 205
Lys Val Ser Phe Asp Pro Ile Pro Leu His Tyr Cys Ala Pro Ala Gly
    210                 215                 220
Tyr Ala Ile Leu Lys Cys Asn Asn Asn Thr Phe Asn Gly Thr Gly Pro
225                 230                 235                 240
Cys Asn Asn Val Ser Thr Ile Gln Cys Thr His Gly Ile Lys Pro Val
                245                 250                 255
Val Ser Thr Gln Leu Leu Leu Asn Gly Ser Arg Ala Glu Lys Glu Ile
            260                 265                 270
Ile Ile Arg Ser Glu Asn Met Thr Asn Asn Ala Lys Thr Ile Ile Val
        275                 280                 285
His Leu Asn Glu Ser Ile Glu Ile Glu Cys Ile Arg Pro Asn Asn Asn
    290                 295                 300
Thr Arg Lys Ser Ile Arg Ile Gly Pro Gly Gln Thr Phe Tyr Ala Thr
305                 310                 315                 320
Asn Gly Met Ile Gly Asp Ile Arg Gln Ala His Cys Asn Ile Ser Gly
                325                 330                 335
Ala Asp Trp Asn Arg Thr Leu Gln Gly Val Gly Arg Lys Leu Ala Gly
            340                 345                 350
Tyr Phe Pro Asn Lys Thr Ile Ser Phe Gln Pro Ser Ser Gly Gly Asp
        355                 360                 365
Leu Glu Ile Thr Thr His Ser Phe Asn Cys Gly Gly Glu Phe Phe Tyr
    370                 375                 380
Cys Asn Thr Ser Ser Leu Phe Asn Asn Thr Tyr Arg Pro Thr Tyr Trp
385                 390                 395                 400
Pro Asn Gly Thr Glu Ser Asn Ser Thr Ile Thr Leu Gln Cys Arg Ile
                405                 410                 415
Lys Gln Ile Ile Asn Met Trp Gln Lys Val Gly Arg Ala Ile Tyr Ala
            420                 425                 430
Pro Pro Ile Ala Gly Lys Ile Thr Cys Lys Ser Asn Ile Thr Gly Leu
        435                 440                 445
Leu Leu Val Arg Asp Gly Gly Asn Gly Gly Asn Asn Thr Ala Thr Glu
    450                 455                 460
Ile Phe Arg Pro Gly Gly Gly Asn Met Lys Asp Asn Trp Arg Ser Glu
465                 470                 475                 480
Leu Tyr Lys Tyr Lys Val Val Glu Ile Lys Pro Leu Gly Ile Ala Pro
                485                 490                 495
Thr Gly Ala Lys Arg Arg Val Val Gly Arg Glu Lys Arg Ala Val Gly
            500                 505                 510
Ile Gly Ala Val Phe Leu Gly Phe Leu Gly Ala Ala Gly Ser Thr Met
        515                 520                 525
Gly Ala Ala Ser Ile Thr Leu Thr Val Gln Ala Arg Gln Leu Leu Ser
    530                 535                 540
Gly Ile Val Gln Gln Gln Ser Asn Leu Leu Lys Ala Ile Glu Ala Gln
545                 550                 555                 560
His His Leu Leu Gln Leu Thr Val Trp Gly Ile Lys Gln Leu Gln Ala
                565                 570                 575
Arg Val Leu Ala Ile Glu Arg Tyr Leu Lys Asp Gln Gln Leu Leu Gly
            580                 585                 590
Ile Trp Gly Cys Ser Gly Lys Leu Ile Cys Thr Thr Ala Val Pro Trp
        595                 600                 605
Asn Ser Ser Trp Ser Asn Lys Ser Gln Ala Asp Ile Trp Asp Asn Met
    610                 615                 620
Thr Trp Met Gln Trp Asp Arg Glu Ile Ser Asn Tyr Thr Asp Thr Ile
625                 630                 635                 640
Tyr Arg Leu Leu Glu Val Ser Gln Thr Gln Gln Glu Gln Asn Glu Gln
                645                 650                 655
Asp Leu Leu Ala Leu Asn Lys Trp Gln His Leu Trp Asn Trp Phe Asp
```

660 665 670
Ile Thr Lys Trp Leu Trp Tyr Ile Lys Ile Phe Ile Met Ile Val Gly
675 680 685
Gly Leu Ile Gly Leu Arg Ile Ile Phe Ala Val Leu Ser Ile Val Asn
690 695 700
Arg Val Arg Gln Gly Tyr Ser Pro Leu Ser Leu Gln Thr Leu Thr Pro
705 710 715 720
Asn Gln Arg Glu Pro Asp Arg Leu Gly Arg Ile Glu Glu Glu Gly Gly
725 730 735
Glu Gln Asp Arg Lys Arg Ser Ile Arg Leu Val Ser Gly Phe Leu Ala
740 745 750
Leu Ala Trp Asp Asp Leu Arg Ser Leu Cys Leu Phe Ser Tyr His His
755 760 765
Leu Arg Asp Phe Ile Leu Ile Ala Ala Arg Val Val Glu Leu Leu Gly
770 775 780
Arg Arg Gly Trp Asp Ile Leu Lys Tyr Leu Ala Ser Leu Val Gln Tyr
785 790 795 800
Trp Gly Leu Glu Leu Lys Lys Gly Ala Ile Ser Leu Leu Asp Ser Ile
805 810 815
Ala Ile Ala Val Ala Glu Gly Thr Asp Arg Ile Ile Ala Phe Ile Gln
820 825 830
Arg Leu Phe Arg Ala Ile Cys Asn Leu Pro Arg Arg Ile Arg Gln Gly
835 840 845
Phe Glu Ala Ser Leu Leu
850

<210> 220
<211> 242
<212> PRT
<213> Human Immunodeficiency Virus

<400> 220
Met Ala Glu Thr Glu Ala Leu Ser Lys Leu Arg Glu Asp Phe Arg Met
1 5 10 15
Gln Asn Lys Ser Val Phe Ile Leu Gly Ala Ser Gly Glu Thr Gly Arg
20 25 30
Val Leu Leu Lys Glu Ile Leu Glu Gln Gly Leu Phe Ser Lys Val Thr
35 40 45
Leu Ile Gly Arg Arg Lys Leu Thr Phe Asp Glu Glu Ala Tyr Lys Asn
50 55 60
Val Asn Gln Glu Val Val Asp Phe Glu Lys Leu Asp Asp Tyr Ala Ser
65 70 75 80
Ala Phe Gln Gly His Asp Val Gly Phe Cys Cys Leu Gly Thr Thr Arg
85 90 95
Gly Lys Ala Gly Ala Glu Gly Phe Val Arg Val Asp Arg Asp Tyr Val
100 105 110
Leu Lys Ser Ala Glu Leu Ala Lys Ala Gly Gly Cys Lys His Phe Asn
115 120 125
Leu Leu Ser Ser Lys Gly Ala Asp Lys Ser Ser Asn Phe Leu Tyr Leu
130 135 140
Gln Val Lys Gly Glu Val Glu Ala Lys Val Glu Glu Leu Lys Phe Asp
145 150 155 160
Arg Tyr Ser Val Phe Arg Pro Gly Val Leu Leu Cys Asp Arg Gln Glu
165 170 175
Ser Arg Pro Gly Glu Trp Leu Val Arg Lys Phe Phe Gly Ser Leu Pro
180 185 190
Asp Ser Trp Ala Arg Gly His Ser Val Pro Val Val Thr Val Val Arg
195 200 205
Ala Met Leu Asn Asn Val Val Arg Pro Arg Asp Lys Gln Met Glu Leu
210 215 220

```
Leu Glu Asn Lys Ala Ile His Asp Leu Gly Lys Ala His Gly Ser Leu
225                 230                 235                 240
Lys Pro
```

<210> 221
<211> 210
<212> PRT
<213> Human Immunodeficiency Virus

<220>
<221> VARIANT
<222> 31, 97, 140, 141, 144, 178
<223> Xaa = Any Amino Acid

<400> 221

```
Cys Thr Glu Met Glu Lys Glu Gly Lys Ile Ser Lys Ile Gly Pro Glu
 1               5                  10                  15
Asn Pro Tyr Asn Thr Pro Val Phe Ala Ile Lys Lys Lys Asp Xaa Thr
            20                  25                  30
Lys Trp Arg Lys Leu Val Asp Phe Arg Glu Leu Asn Lys Arg Thr Gln
        35                  40                  45
Asp Phe Trp Glu Val Gln Leu Gly Ile Pro His Pro Ala Gly Leu Lys
    50                  55                  60
Lys Lys Lys Ser Val Thr Val Leu Asp Val Gly Asp Ala Tyr Phe Ser
65                  70                  75                  80
Val Pro Leu Asp Glu Ser Phe Arg Lys Tyr Thr Ala Phe Thr Ile Pro
                85                  90                  95
Xaa Thr Asn Asn Glu Thr Pro Gly Ile Arg Tyr Gln Tyr Asn Val Leu
            100                 105                 110
Pro Gln Gly Trp Lys Gly Ser Pro Ala Ile Phe Gln Ser Ser Met Thr
        115                 120                 125
Lys Ile Leu Glu Pro Phe Arg Ile Lys Asn Pro Xaa Xaa Val Ile Xaa
    130                 135                 140
Gln Tyr Met Asp Asp Leu Tyr Val Gly Ser Asp Leu Glu Ile Gly Gln
145                 150                 155                 160
His Arg Ala Lys Ile Glu Glu Leu Arg Lys His Leu Leu Ser Trp Gly
                165                 170                 175
Phe Xaa Thr Pro Asp Lys Lys His Gln Lys Glu Pro Pro Phe Leu Trp
            180                 185                 190
Met Gly Tyr Glu Leu His Pro Asp Lys Trp Thr Val Gln Pro Ile Gln
        195                 200                 205
Leu Pro
    210
```

<210> 222
<211> 207
<212> PRT
<213> Human Immunodeficiency Virus

<400> 222

```
Met Gly Gly Lys Trp Ser Lys Ser Ser Leu Val Gly Trp Pro Glu Val
 1               5                  10                  15
Arg Asp Arg Ile Arg Arg Thr Asp Pro Ala Ala Glu Gly Val Gly Ala
            20                  25                  30
Ala Ser Gln Asp Leu Asp Lys His Gly Ala Leu Thr Asn Ser Asn Thr
        35                  40                  45
Ala Ala Thr Asn Lys Asp Cys Ala Trp Leu Glu Ala Gln Glu Glu Glu
    50                  55                  60
```

```
Gly Glu Val Gly Phe Pro Val Arg Pro Gln Val Pro Leu Arg Pro Met
65                  70                  75                  80
Thr Tyr Lys Gly Ala Phe Asp Leu Gly Trp Phe Leu Lys Glu Lys Gly
                85                  90                  95
Gly Leu Asp Gly Leu Ile Tyr Ser Lys Lys Arg Gln Glu Ile Leu Asp
            100                 105                 110
Leu Trp Val Tyr His Thr Gln Gly Tyr Phe Pro Asp Trp Gln Asn Tyr
        115                 120                 125
Thr Pro Gly Pro Gly Val Arg Tyr Pro Leu Thr Phe Gly Trp Cys Tyr
    130                 135                 140
Lys Leu Val Pro Val Asp Pro Lys Glu Val Glu Glu Ala Thr Glu Gly
145                 150                 155                 160
Glu Asn Asn Cys Leu Leu His Pro Ile Cys Gln His Gly Met Glu Asp
                165                 170                 175
Glu Asp Arg Glu Val Leu Arg Trp Lys Phe Asp Ser Glu Leu Ala Arg
            180                 185                 190
Arg His Ile Ala Arg Glu Arg His Pro Glu Phe Tyr Lys Asp Cys
        195                 200                 205
```

<210> 223
<211> 397
<212> PRT
<213> Plasmodium falciparum

<400> 223

```
Met Met Arg Lys Leu Ala Ile Leu Ser Val Ser Ser Phe Leu Phe Val
 1               5                  10                  15
Glu Ala Leu Phe Gln Glu Tyr Gln Cys Tyr Gly Ser Ser Ser Asn Thr
            20                  25                  30
Arg Val Leu Asn Glu Leu Asn Tyr Asp Asn Ala Gly Thr Asn Leu Tyr
        35                  40                  45
Asn Glu Leu Glu Met Asn Tyr Tyr Gly Lys Gln Glu Asn Trp Tyr Ser
    50                  55                  60
Leu Lys Lys Asn Ser Arg Ser Leu Gly Glu Asn Asp Asp Gly Asn Asn
65                  70                  75                  80
Glu Asp Asn Glu Lys Leu Arg Lys Pro Lys His Lys Lys Leu Lys Gln
                85                  90                  95
Pro Ala Asp Gly Asn Pro Asp Pro Asn Ala Asn Pro Asn Val Asp Pro
            100                 105                 110
Asn Ala Asn Pro Asn Val Asp Pro Asn Ala Asn Pro Asn Val Asp Pro
        115                 120                 125
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
    130                 135                 140
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
145                 150                 155                 160
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
                165                 170                 175
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
            180                 185                 190
Asn Ala Asn Pro Asn Val Asp Pro Asn Ala Asn Pro Asn Ala Asn Pro
        195                 200                 205
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
    210                 215                 220
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
225                 230                 235                 240
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
                245                 250                 255
Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
            260                 265                 270
Asn Lys Asn Asn Gln Gly Asn Gly Gln Gly His Asn Met Pro Asn Asp
```

```
        275                 280                 285
Pro Asn Arg Asn Val Asp Glu Asn Ala Asn Ala Asn Ser Ala Val Lys
    290                 295                 300
Asn Asn Asn Asn Glu Glu Pro Ser Asp Lys His Ile Lys Glu Tyr Leu
305                 310                 315                 320
Asn Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro Cys Ser Val
                325                 330                 335
Thr Cys Gly Asn Gly Ile Gln Val Arg Ile Lys Pro Gly Ser Ala Asn
            340                 345                 350
Lys Pro Lys Asp Glu Leu Asp Tyr Ala Asn Asp Ile Glu Lys Lys Ile
        355                 360                 365
Cys Lys Met Glu Lys Cys Ser Ser Val Phe Asn Val Val Asn Ser Ser
    370                 375                 380
Ile Gly Leu Ile Met Val Leu Ser Phe Leu Phe Leu Asn
385                 390                 395


<210> 224
<211> 69
<212> PRT
<213> Plasmodium falciparum

<400> 224
Thr Glu Trp Ser Pro Cys Ser Val Thr Cys Gly Asn Gly Ile Gln Val
 1                   5                  10                  15
Arg Ile Lys Pro Gly Ser Ala Asn Lys Pro Lys Asp Glu Leu Asp Tyr
            20                  25                  30
Glu Asn Asp Ile Glu Lys Lys Ile Cys Lys Met Glu Lys Cys Ser Ser
        35                  40                  45
Val Phe Asn Val Val Asn Ser Ser Ile Gly Leu Ile Met Val Leu Ser
    50                  55                  60
Phe Leu Phe Leu Asn
65


<210> 225
<211> 137
<212> PRT
<213> Salmonella enterica

<400> 225
Met Tyr Met Ser Lys Tyr Val Pro Val Tyr Thr Leu Leu Ile Leu Ile
 1                   5                  10                  15
Tyr Ser Phe Asn Ala Ser Ala Glu Trp Thr Gly Asp Asn Thr Asn Ala
            20                  25                  30
Tyr Tyr Ser Asp Glu Val Ile Ser Glu Leu His Val Gly Gln Ile Asp
        35                  40                  45
Thr Ser Pro Tyr Phe Cys Ile Lys Thr Val Lys Ala Asn Gly Ser Gly
    50                  55                  60
Thr Pro Val Val Ala Cys Ala Val Ser Lys Gln Ser Ile Trp Ala Pro
65                  70                  75                  80
Ser Phe Lys Glu Leu Leu Asp Gln Ala Arg Tyr Phe Tyr Ser Thr Gly
                85                  90                  95
Gln Ser Val Arg Ile His Val Gln Lys Asn Ile Trp Thr Tyr Pro Leu
            100                 105                 110
Phe Val Asn Thr Phe Ser Ala Asn Ala Leu Val Gly Leu Ser Ser Cys
        115                 120                 125
Ser Ala Thr Gln Cys Phe Gly Pro Lys
    130                 135
```

<210> 226
<211> 233
<212> PRT
<213> Staphylococcus aureus

<400> 226
Ser Glu Lys Ser Glu Glu Ile Asn Glu Lys Asp Leu Arg Lys Lys Ser
1 5 10 15
Glu Leu Gln Gly Thr Ala Leu Gly Asn Leu Lys Gln Ile Tyr Tyr Tyr
20 25 30
Asn Glu Lys Ala Lys Thr Glu Asn Lys Glu Ser His Asp Gln Phe Leu
35 40 45
Gln His Thr Ile Leu Phe Lys Gly Phe Phe Thr Asp His Ser Trp Tyr
50 55 60
Asn Asp Leu Leu Val Asp Phe Asp Ser Lys Asp Ile Val Asp Lys Tyr
65 70 75 80
Lys Gly Lys Lys Val Asp Leu Tyr Gly Ala Tyr Tyr Gly Tyr Gln Cys
85 90 95
Ala Gly Gly Thr Pro Asn Lys Thr Ala Cys Met Tyr Gly Gly Val Thr
100 105 110
Leu His Asp Asn Asn Arg Leu Thr Glu Glu Lys Lys Val Pro Ile Asn
115 120 125
Leu Trp Leu Asp Gly Lys Gln Asn Thr Val Pro Leu Glu Thr Val Lys
130 135 140
Thr Asn Lys Lys Asn Val Thr Val Gln Glu Leu Asp Leu Gln Ala Arg
145 150 155 160
Arg Tyr Leu Gln Glu Lys Tyr Asn Leu Tyr Asn Ser Asp Val Phe Asp
165 170 175
Gly Lys Val Gln Arg Gly Leu Ile Val Phe His Thr Ser Thr Glu Pro
180 185 190
Ser Val Asn Tyr Asp Leu Phe Gly Ala Gln Gly Gln Tyr Ser Asn Thr
195 200 205
Leu Leu Arg Ile Tyr Arg Asp Asn Lys Ser Ile Asn Ser Glu Asn Met
210 215 220
His Ile Asp Ile Tyr Leu Tyr Thr Ser
225 230

<210> 227
<211> 68
<212> PRT
<213> Escherichia coli

<400> 227
Ala Trp Arg Glu Glu Pro Trp Ile His His Ala Pro Gln Gly Cys Gly
1 5 10 15
Asp Ser Ser Arg Thr Ile Thr Gly Asp Thr Cys Asn Glu Glu Thr Gln
20 25 30
Asn Leu Ser Thr Ile Tyr Leu Arg Lys Tyr Gln Ser Lys Val Lys Arg
35 40 45
Gln Ile Phe Ser Asp Tyr Gln Ser Glu Val Asp Ile Tyr Asn Arg Ile
50 55 60
Arg Asn Glu Leu
65

<210> 228
<211> 396
<212> PRT
<213> Clostridium difficile

<400> 228
Asn Glu Tyr Tyr Pro Glu Ile Ile Val Leu Asn Pro Asn Thr Phe His
1 5 10 15
Lys Lys Val Asn Ile Asn Leu Asp Ser Ser Ser Phe Glu Tyr Lys Trp
20 25 30
Ser Thr Glu Gly Ser Asp Phe Ile Leu Val Arg Tyr Leu Glu Glu Ser
35 40 45
Asn Lys Lys Ile Leu Gln Lys Ile Arg Ile Lys Gly Ile Leu Ser Asn
50 55 60
Thr Lys Ser Phe Asn Lys Met Ser Ile Asp Phe Lys Asp Ile Lys Lys
65 70 75 80
Leu Ser Leu Gly Tyr Ile Met Ser Asn Phe Lys Ser Phe Asn Ser Glu
85 90 95
Asn Glu Leu Asp Arg Asp His Leu Gly Phe Lys Ile Ile Asp Asn Lys
100 105 110
Thr Tyr Tyr Tyr Asp Glu Ala Ser Lys Leu Val Lys Gly Leu Ile Asn
115 120 125
Ile Asn Asn Ser Leu Phe Tyr Phe Asp Pro Ile Glu Ser Asn Leu Val
130 135 140
Thr Gly Trp Gln Thr Ile Asn Gly Lys Lys Tyr Tyr Phe Asp Ile Asn
145 150 155 160
Thr Gly Ala Ala Ser Thr Ser Tyr Lys Ile Ile Asn Gly Lys His Phe
165 170 175
Tyr Phe Asn Asn Asn Gly Val Met Gln Leu Gly Val Phe Lys Gly Pro
180 185 190
Asp Gly Phe Glu Tyr Phe Ala Pro Ala Asn Thr Gln Asn Asn Asn Ile
195 200 205
Glu Gly Gln Ala Ile Val Tyr Gln Ser Lys Phe Leu Thr Leu Asn Gly
210 215 220
Lys Lys Tyr Tyr Phe Asp Asn Asp Ser Lys Ala Val Thr Gly Trp Gln
225 230 235 240
Thr Ile Asp Gly Lys Lys Tyr Tyr Phe Asn Leu Asn Thr Ala Glu Ala
245 250 255
Ala Thr Gly Trp Gln Thr Ile Asp Gly Lys Lys Tyr Tyr Phe Asn Thr
260 265 270
Asn Thr Ser Ile Ala Ser Thr Gly Tyr Thr Ile Ile Asn Gly Lys His
275 280 285
Phe Tyr Phe Asn Thr Asp Gly Ile Met Gln Ile Gly Val Phe Lys Gly
290 295 300
Pro Asn Gly Phe Glu Tyr Phe Ala Pro Ala Asn Thr Asp Ala Asn Asn
305 310 315 320
Ile Glu Gly Gln Ala Ile Arg Tyr Gln Asn Arg Phe Leu Tyr Leu His
325 330 335
Asp Asn Ile Tyr Tyr Phe Gly Asn Asn Ser Lys Ala Val Thr Gly Trp
340 345 350
Gln Thr Ile Asn Gly Asn Val Tyr Tyr Phe Met Pro Asp Thr Ala Met
355 360 365
Ala Ala Ala Gly Gly Leu Phe Glu Ile Asp Gly Val Ile Tyr Phe Phe
370 375 380
Gly Val Asp Gly Val Lys Ala Pro Gly Ile Tyr Gly
385 390 395

<210> 229
<211> 386
<212> PRT
<213> Bacillus cereus

<400> 229
Met Lys Lys Thr Leu Ile Thr Gly Leu Leu Val Thr Ala Val Ser Thr
1 5 10 15

```
Ser Arg Phe Ile Pro Val Ser Ala Tyr Ala Lys Glu Gly Gln Thr Glu
            20                  25                  30
Val Lys Thr Val Tyr Ala Gln Asn Val Ile Ala Pro Asn Thr Leu Ser
        35                  40                  45
Asn Ser Ile Arg Met Leu Gly Ser Gln Ser Pro Leu Ile Gln Ala Tyr
    50                  55                  60
Gly Leu Ile Ile Leu Gln Gln Pro Asp Ile Lys Val Asn Ala Met Ser
65                  70                  75                  80
Ser Leu Thr Asn His Gln Lys Phe Ala Lys Ala Asn Val Arg Glu Trp
                85                  90                  95
Ile Asp Glu Tyr Asn Pro Lys Leu Ile Asp Leu Asn Gln Glu Met Met
            100                 105                 110
Arg Tyr Ser Thr Arg Phe Asn Ser Tyr Tyr Ser Lys Leu Tyr Glu Leu
        115                 120                 125
Ala Gly Asn Val Asn Glu Asp Gln Gln Ala Lys Ala Asp Phe Met Ser
    130                 135                 140
Ala Tyr Gly Lys Leu Gln Leu Gln Val Gln Ser Ile Gln Glu Ser Met
145                 150                 155                 160
Glu Gln Asp Leu Leu Glu Leu Asn Arg Phe Lys Thr Val Leu Asp Lys
                165                 170                 175
Asp Ser Asn Asn Leu Ser Ile Lys Ala Asp Glu Ala Ile Lys Thr Leu
            180                 185                 190
Gln Gly Ser Ser Gly Asp Ile Val Lys Leu Arg Glu Asp Ile Lys Arg
        195                 200                 205
Ile Gln Gly Glu Ile Gln Ala Glu Leu Thr Thr Ile Leu Asn Arg Pro
    210                 215                 220
Gln Glu Ile Ile Lys Gly Ser Ile Asn Ile Gly Lys Gln Val Phe Thr
225                 230                 235                 240
Ile Thr Asn Gln Thr Ala Gln Thr Lys Thr Ile Asp Phe Val Ser Ile
                245                 250                 255
Gly Thr Leu Ser Asn Glu Ile Val Asn Ala Ala Asp Ser Gln Thr Arg
            260                 265                 270
Glu Ala Ala Leu Arg Ile Gln Gln Lys Gln Lys Glu Leu Leu Pro Leu
        275                 280                 285
Ile Gln Lys Leu Ser Gln Thr Glu Ala Glu Ala Thr Gln Ile Thr Phe
    290                 295                 300
Val Glu Asp Gln Val Asn Ser Phe Thr Glu Leu Ile Asp Arg Gln Ile
305                 310                 315                 320
Thr Thr Leu Glu Thr Leu Leu Thr Asp Trp Lys Val Leu Asn Asn Asn
                325                 330                 335
Met Ile Gln Ile Gln Lys Asn Val Glu Glu Gly Thr Tyr Thr Asp Ser
            340                 345                 350
Ser Leu Leu Gln Lys His Phe Asn Gln Ile Lys Lys Val Ser Asp Glu
        355                 360                 365
Met Asn Lys Gln Thr Asn Gln Phe Glu Asp Tyr Val Thr Asn Val Glu
    370                 375                 380
Val His
385
```

<210> 230
<211> 227
<212> PRT
<213> Bordetella pertussis

<400> 230

```
Met Leu Ile Asn Asn Lys Lys Leu Leu His His Ile Leu Pro Ile Leu
 1               5                  10                  15
Val Leu Ala Leu Leu Gly Met Arg Thr Ala Gln Ala Val Ala Pro Gly
            20                  25                  30
Ile Val Ile Pro Pro Lys Ala Leu Phe Thr Gln Gln Gly Gly Ala Tyr
```

```
        35                  40                  45
Gly Arg Cys Pro Asn Gly Thr Arg Ala Leu Thr Val Ala Glu Leu Arg
    50                  55                  60
Gly Asn Ala Glu Leu Gln Thr Tyr Leu Arg Gln Ile Thr Pro Gly Trp
65                  70                  75                  80
Ser Ile Tyr Gly Leu Tyr Asp Gly Thr Tyr Leu Gly Gln Ala Tyr Gly
                85                  90                  95
Gly Ile Ile Lys Asp Ala Pro Pro Gly Ala Gly Phe Ile Tyr Arg Glu
            100                 105                 110
Thr Phe Cys Ile Thr Thr Ile Tyr Lys Thr Gly Gln Pro Ala Ala Asp
        115                 120                 125
His Tyr Tyr Ser Lys Val Thr Ala Thr Arg Leu Leu Ala Ser Thr Asn
    130                 135                 140
Ser Arg Leu Cys Ala Val Phe Val Arg Asp Gly Gln Ser Val Ile Gly
145                 150                 155                 160
Ala Cys Ala Ser Pro Tyr Glu Gly Arg Tyr Arg Asp Met Tyr Asp Ala
                165                 170                 175
Leu Arg Arg Leu Leu Tyr Met Ile Tyr Met Ser Gly Leu Ala Val Arg
            180                 185                 190
Val His Val Ser Lys Glu Glu Gln Tyr Tyr Asp Tyr Glu Asp Ala Thr
        195                 200                 205
Phe Gln Thr Tyr Ala Leu Thr Gly Ile Ser Leu Cys Asn Pro Ala Ala
    210                 215                 220
Ser Ile Cys
225
```

<210> 231
<211> 76
<212> PRT
<213> SARS coronavirus

<400> 231

```
Met Tyr Ser Phe Val Ser Glu Glu Thr Gly Thr Leu Ile Val Asn Ser
 1               5                  10                  15
Val Leu Leu Phe Leu Ala Phe Val Val Phe Leu Leu Val Thr Leu Ala
            20                  25                  30
Ile Leu Thr Ala Leu Arg Leu Cys Ala Tyr Cys Cys Asn Ile Val Asn
        35                  40                  45
Val Ser Leu Val Lys Pro Thr Val Tyr Val Tyr Ser Arg Val Lys Asn
    50                  55                  60
Leu Asn Ser Ser Glu Gly Val Pro Asp Leu Leu Val
65                  70                  75
```

<210> 232
<211> 125
<212> PRT
<213> Homo sapiens

<400> 232

```
Gln Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly
 1               5                  10                  15
Phe Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val
            20                  25                  30
Gln Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys
        35                  40                  45
Ala Ala Pro Ser Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu
    50                  55                  60
Arg Glu Asp Gln Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr
```

65 70 75 80
Tyr Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys
85 90 95
Asp Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn
100 105 110
Ile Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser
115 120 125

<210> 233
<211> 221
<212> PRT
<213> SARS coronavirus

<400> 233
Met Ala Asp Asn Gly Thr Ile Thr Val Glu Glu Leu Lys Gln Leu Leu
1 5 10 15
Glu Gln Trp Asn Leu Val Ile Gly Phe Leu Phe Leu Ala Trp Ile Met
20 25 30
Leu Leu Gln Phe Ala Tyr Ser Asn Arg Asn Arg Phe Leu Tyr Ile Ile
35 40 45
Lys Leu Val Phe Leu Trp Leu Leu Trp Pro Val Thr Leu Ala Cys Phe
50 55 60
Val Leu Ala Ala Val Tyr Arg Ile Asn Trp Val Thr Gly Gly Ile Ala
65 70 75 80
Ile Ala Met Ala Cys Ile Val Gly Leu Met Trp Leu Ser Tyr Phe Val
85 90 95
Ala Ser Phe Arg Leu Phe Ala Arg Thr Arg Ser Met Trp Ser Phe Asn
100 105 110
Pro Glu Thr Asn Ile Leu Leu Asn Val Pro Leu Arg Gly Thr Ile Val
115 120 125
Thr Arg Pro Leu Met Glu Ser Glu Leu Val Ile Gly Ala Val Ile Ile
130 135 140
Arg Gly His Leu Arg Met Ala Gly His Ser Leu Gly Arg Cys Asp Ile
145 150 155 160
Lys Asp Leu Pro Lys Glu Ile Thr Val Ala Thr Ser Arg Thr Leu Ser
165 170 175
Tyr Tyr Lys Leu Gly Ala Ser Gln Arg Val Gly Thr Asp Ser Gly Phe
180 185 190
Ala Ala Tyr Asn Arg Tyr Arg Ile Gly Asn Tyr Lys Leu Asn Thr Asp
195 200 205
His Ala Gly Ser Asn Asp Asn Ile Ala Leu Leu Val Gln
210 215 220

<210> 234
<211> 422
<212> PRT
<213> SARS coronavirus

<400> 234
Met Ser Asp Asn Gly Pro Gln Ser Asn Gln Arg Ser Ala Pro Arg Ile
1 5 10 15
Thr Phe Gly Gly Pro Thr Asp Ser Thr Asp Asn Asn Gln Asn Gly Gly
20 25 30
Arg Asn Gly Ala Arg Pro Lys Gln Arg Arg Pro Gln Gly Leu Pro Asn
35 40 45
Asn Thr Ala Ser Trp Phe Thr Ala Leu Thr Gln His Gly Lys Glu Glu
50 55 60
Leu Arg Phe Pro Arg Gly Gln Gly Val Pro Ile Asn Thr Asn Ser Gly
65 70 75 80

```
Pro Asp Asp Gln Ile Gly Tyr Tyr Arg Arg Ala Thr Arg Arg Val Arg
                85                  90                  95
Gly Gly Asp Gly Lys Met Lys Glu Leu Ser Pro Arg Trp Tyr Phe Tyr
            100                 105                 110
Tyr Leu Gly Thr Gly Pro Glu Ala Ser Leu Pro Tyr Gly Ala Asn Lys
        115                 120                 125

Glu Gly Ile Val Trp Val Ala Thr Glu Gly Ala Leu Asn Thr Pro Lys
    130                 135                 140
Asp His Ile Gly Thr Arg Asn Pro Asn Asn Asn Ala Ala Thr Val Leu
145                 150                 155                 160
Gln Leu Pro Gln Gly Thr Thr Leu Pro Lys Gly Phe Tyr Ala Glu Gly
                165                 170                 175
Ser Arg Gly Gly Ser Gln Ala Ser Ser Arg Ser Ser Ser Arg Ser Arg
            180                 185                 190
Gly Asn Ser Arg Asn Ser Thr Pro Gly Ser Ser Arg Gly Asn Ser Pro
        195                 200                 205
Ala Arg Met Ala Ser Gly Gly Gly Glu Thr Ala Leu Ala Leu Leu Leu
    210                 215                 220
Leu Asp Arg Leu Asn Gln Leu Glu Ser Lys Val Ser Gly Lys Gly Gln
225                 230                 235                 240
Gln Gln Gln Gly Gln Thr Val Thr Lys Lys Ser Ala Ala Glu Ala Ser
                245                 250                 255
Lys Lys Pro Arg Gln Lys Arg Thr Ala Thr Lys Gln Tyr Asn Val Thr
            260                 265                 270
Gln Ala Phe Gly Arg Arg Gly Pro Glu Gln Thr Gln Gly Asn Phe Gly
        275                 280                 285
Asp Gln Asp Leu Ile Arg Gln Gly Thr Asp Tyr Lys His Trp Pro Gln
    290                 295                 300
Ile Ala Gln Phe Ala Pro Ser Ala Ser Ala Phe Phe Gly Met Ser Arg
305                 310                 315                 320
Ile Gly Met Glu Val Thr Pro Ser Gly Thr Trp Leu Thr Tyr His Gly
                325                 330                 335
Ala Ile Lys Leu Asp Asp Lys Asp Pro Gln Phe Lys Asp Asn Val Ile
            340                 345                 350
Leu Leu Asn Lys His Ile Asp Ala Tyr Lys Thr Phe Pro Pro Thr Glu
        355                 360                 365
Pro Lys Lys Asp Lys Lys Lys Lys Thr Asp Glu Ala Gln Pro Leu Pro
    370                 375                 380
Gln Arg Gln Lys Lys Gln Pro Thr Val Thr Leu Leu Pro Ala Ala Asp
385                 390                 395                 400
Met Asp Asp Phe Ser Arg Gln Leu Gln Asn Ser Met Ser Gly Ala Ser
                405                 410                 415
Ala Asp Ser Thr Gln Ala
            420
```

<210> 235
<211> 1255
<212> PRT
<213> Human Immunodeficiency Virus

<400> 235

```
Met Phe Ile Phe Leu Leu Phe Leu Thr Leu Thr Ser Gly Ser Asp Leu
 1               5                  10                  15
Asp Arg Cys Thr Thr Phe Asp Asp Val Gln Ala Pro Asn Tyr Thr Gln
            20                  25                  30
His Thr Ser Ser Met Arg Gly Val Tyr Tyr Pro Asp Glu Ile Phe Arg
        35                  40                  45
Ser Asp Thr Leu Tyr Leu Thr Gln Asp Leu Phe Leu Pro Phe Tyr Ser
    50                  55                  60
```

```
Asn Val Thr Gly Phe His Thr Ile Asn His Thr Phe Gly Asn Pro Val
65                  70                  75                  80
Ile Pro Phe Lys Asp Gly Ile Tyr Phe Ala Ala Thr Glu Lys Ser Asn
                85                  90                  95
Val Val Arg Gly Trp Val Phe Gly Ser Thr Met Asn Asn Lys Ser Gln
            100                 105                 110
Ser Val Ile Ile Ile Asn Asn Ser Thr Asn Val Val Ile Arg Ala Cys
        115                 120                 125
Asn Phe Glu Leu Cys Asp Asn Pro Phe Phe Ala Val Ser Lys Pro Met
    130                 135                 140
Gly Thr Gln Thr His Thr Met Ile Phe Asp Asn Ala Phe Asn Cys Thr
145                 150                 155                 160
Phe Glu Tyr Ile Ser Asp Ala Phe Ser Leu Asp Val Ser Glu Lys Ser
                165                 170                 175
Gly Asn Phe Lys His Leu Arg Glu Phe Val Phe Lys Asn Lys Asp Gly
            180                 185                 190
Phe Leu Tyr Val Tyr Lys Gly Tyr Gln Pro Ile Asp Val Val Arg Asp
        195                 200                 205
Leu Pro Ser Gly Phe Asn Thr Leu Lys Pro Ile Phe Lys Leu Pro Leu
    210                 215                 220
Gly Ile Asn Ile Thr Asn Phe Arg Ala Ile Leu Thr Ala Phe Ser Pro
225                 230                 235                 240
Ala Gln Asp Ile Trp Gly Thr Ser Ala Ala Ala Tyr Phe Val Gly Tyr
                245                 250                 255
Leu Lys Pro Thr Thr Phe Met Leu Lys Tyr Asp Glu Asn Gly Thr Ile
            260                 265                 270
Thr Asp Ala Val Asp Cys Ser Gln Asn Pro Leu Ala Glu Leu Lys Cys
        275                 280                 285
Ser Val Lys Ser Phe Glu Ile Asp Lys Gly Ile Tyr Gln Thr Ser Asn
    290                 295                 300
Phe Arg Val Val Pro Ser Gly Asp Val Val Arg Phe Pro Asn Ile Thr
305                 310                 315                 320
Asn Leu Cys Pro Phe Gly Glu Val Phe Asn Ala Thr Lys Phe Pro Ser
                325                 330                 335
Val Tyr Ala Trp Glu Arg Lys Lys Ile Ser Asn Cys Val Ala Asp Tyr
            340                 345                 350
Ser Val Leu Tyr Asn Ser Thr Phe Phe Ser Thr Phe Lys Cys Tyr Gly
        355                 360                 365
Val Ser Ala Thr Lys Leu Asn Asp Leu Cys Phe Ser Asn Val Tyr Ala
    370                 375                 380
Asp Ser Phe Val Val Lys Gly Asp Asp Val Arg Gln Ile Ala Pro Gly
385                 390                 395                 400
Gln Thr Gly Val Ile Ala Asp Tyr Asn Tyr Lys Leu Pro Asp Asp Phe
                405                 410                 415
Met Gly Cys Val Leu Ala Trp Asn Thr Arg Asn Ile Asp Ala Thr Ser
            420                 425                 430
Thr Gly Asn Tyr Asn Tyr Lys Tyr Arg Tyr Leu Arg His Gly Lys Leu
        435                 440                 445
Arg Pro Phe Glu Arg Asp Ile Ser Asn Val Pro Phe Ser Pro Asp Gly
    450                 455                 460
Lys Pro Cys Thr Pro Pro Ala Leu Asn Cys Tyr Trp Pro Leu Asn Asp
465                 470                 475                 480
Tyr Gly Phe Tyr Thr Thr Thr Gly Ile Gly Tyr Gln Pro Tyr Arg Val
                485                 490                 495
Val Val Leu Ser Phe Glu Leu Leu Asn Ala Pro Ala Thr Val Cys Gly
            500                 505                 510
Pro Lys Leu Ser Thr Asp Leu Ile Lys Asn Gln Cys Val Asn Phe Asn
        515                 520                 525
Phe Asn Gly Leu Thr Gly Thr Gly Val Leu Thr Pro Ser Ser Lys Arg
    530                 535                 540
Phe Gln Pro Phe Gln Gln Phe Gly Arg Asp Val Ser Asp Phe Thr Asp
```

545 550 555 560
Ser Val Arg Asp Pro Lys Thr Ser Glu Ile Leu Asp Ile Ser Pro Cys
565 570 575
Ser Phe Gly Gly Val Ser Val Ile Thr Pro Gly Thr Asn Ala Ser Ser
580 585 590
Glu Val Ala Val Leu Tyr Gln Asp Val Asn Cys Thr Asp Val Ser Thr
595 600 605
Ala Ile His Ala Asp Gln Leu Thr Pro Ala Trp Arg Ile Tyr Ser Thr
610 615 620
Gly Asn Asn Val Phe Gln Thr Gln Ala Gly Cys Leu Ile Gly Ala Glu
625 630 635 640
His Val Asp Thr Ser Tyr Glu Cys Asp Ile Pro Ile Gly Ala Gly Ile
645 650 655
Cys Ala Ser Tyr His Thr Val Ser Leu Leu Arg Ser Thr Ser Gln Lys
660 665 670
Ser Ile Val Ala Tyr Thr Met Ser Leu Gly Ala Asp Ser Ser Ile Ala
675 680 685
Tyr Ser Asn Asn Thr Ile Ala Ile Pro Thr Asn Phe Ser Ile Ser Ile
690 695 700
Thr Thr Glu Val Met Pro Val Ser Met Ala Lys Thr Ser Val Asp Cys
705 710 715 720
Asn Met Tyr Ile Cys Gly Asp Ser Thr Glu Cys Ala Asn Leu Leu Leu
725 730 735
Gln Tyr Gly Ser Phe Cys Thr Gln Leu Asn Arg Ala Leu Ser Gly Ile
740 745 750
Ala Ala Glu Gln Asp Arg Asn Thr Arg Glu Val Phe Ala Gln Val Lys
755 760 765
Gln Met Tyr Lys Thr Pro Thr Leu Lys Tyr Phe Gly Gly Phe Asn Phe
770 775 780
Ser Gln Ile Leu Pro Asp Pro Leu Lys Pro Thr Lys Arg Ser Phe Ile
785 790 795 800
Glu Asp Leu Leu Phe Asn Lys Val Thr Leu Ala Asp Ala Gly Phe Met
805 810 815
Lys Gln Tyr Gly Glu Cys Leu Gly Asp Ile Asn Ala Arg Asp Leu Ile
820 825 830
Cys Ala Gln Lys Phe Asn Gly Leu Thr Val Leu Pro Pro Leu Leu Thr
835 840 845
Asp Asp Met Ile Ala Ala Tyr Thr Ala Ala Leu Val Ser Gly Thr Ala
850 855 860
Thr Ala Gly Trp Thr Phe Gly Ala Gly Ala Ala Leu Gln Ile Pro Phe
865 870 875 880
Ala Met Gln Met Ala Tyr Arg Phe Asn Gly Ile Gly Val Thr Gln Asn
885 890 895
Val Leu Tyr Glu Asn Gln Lys Gln Ile Ala Asn Gln Phe Asn Lys Ala
900 905 910
Ile Ser Gln Ile Gln Glu Ser Leu Thr Thr Thr Ser Thr Ala Leu Gly
915 920 925
Lys Leu Gln Asp Val Val Asn Gln Asn Ala Gln Ala Leu Asn Thr Leu
930 935 940
Val Lys Gln Leu Ser Ser Asn Phe Gly Ala Ile Ser Ser Val Leu Asn
945 950 955 960
Asp Ile Leu Ser Arg Leu Asp Lys Val Glu Ala Glu Val Gln Ile Asp
965 970 975
Arg Leu Ile Thr Gly Arg Leu Gln Ser Leu Gln Thr Tyr Val Thr Gln
980 985 990
Gln Leu Ile Arg Ala Ala Glu Ile Arg Ala Ser Ala Asn Leu Ala Ala
995 1000 1005
Thr Lys Met Ser Glu Cys Val Leu Gly Gln Ser Lys Arg Val Asp Phe
1010 1015 1020
Cys Gly Lys Gly Tyr His Leu Met Ser Phe Pro Gln Ala Ala Pro His
1025 1030 1035 1040

Gly Val Val Phe Leu His Val Thr Tyr Val Pro Ser Gln Glu Arg Asn
1045 1050 1055
Phe Thr Thr Ala Pro Ala Ile Cys His Glu Gly Lys Ala Tyr Phe Pro
1060 1065 1070
Arg Glu Gly Val Phe Val Phe Asn Gly Thr Ser Trp Phe Ile Thr Gln
1075 1080 1085
Arg Asn Phe Phe Ser Pro Gln Ile Ile Thr Thr Asp Asn Thr Phe Val
1090 1095 1100
Ser Gly Asn Cys Asp Val Val Ile Gly Ile Ile Asn Asn Thr Val Tyr
1105 1110 1115 1120
Asp Pro Leu Gln Pro Glu Leu Asp Ser Phe Lys Glu Glu Leu Asp Lys
1125 1130 1135
Tyr Phe Lys Asn His Thr Ser Pro Asp Val Asp Phe Gly Asp Ile Ser
1140 1145 1150
Gly Ile Asn Ala Ser Val Val Asn Ile Gln Lys Glu Ile Asp Arg Leu
1155 1160 1165
Asn Glu Val Ala Lys Asn Leu Asn Glu Ser Leu Ile Asp Leu Gln Glu
1170 1175 1180
Leu Gly Lys Tyr Glu Gln Tyr Ile Lys Trp Pro Trp Tyr Val Trp Leu
1185 1190 1195 1200
Gly Phe Ile Ala Gly Leu Ile Ala Ile Val Met Val Thr Ile Leu Leu
1205 1210 1215
Cys Cys Met Thr Ser Cys Cys Ser Cys Leu Lys Gly Ala Cys Ser Cys
1220 1225 1230
Gly Ser Cys Cys Lys Phe Asp Glu Asp Asp Ser Glu Pro Val Leu Lys
1235 1240 1245
Gly Val Lys Leu His Tyr Thr
1250 1255

<210> 236
<211> 28
<212> PRT
<213> Human Immunodeficiency Virus

<400> 236
Asx Thr Thr Met Phe Phe Arg Met Pro Gln Asp Leu Asn Thr Met Leu
1 5 10 15
Asn Thr Val Gly Gly His Gln Ala Ala Met Gln Met
20 25

<210> 237
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 237
Pro Gln Asp Leu Asn Thr Met Leu Asn Thr Val Gly Gly His Gln Ala
1 5 10 15
Ala Met Gln Met
20

<210> 238
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 238
Gly Pro Ile Ala Pro Gly Gln Met Arg Glu Pro Arg Gly Ser Asp Ile

```
 1               5                   10                  15
Ala Gly Thr Thr
            20
```

<210> 239
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 239

```
Gly Pro Ile Ala Pro Gly Gln Met Arg Glu Pro Arg Gly Ser Asp Ile
 1               5                   10                  15
Ala Gly Thr Thr
            20
```

<210> 240
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 240

```
Lys Gly Cys Trp Lys Cys Gly Lys Glu Gly His Gln Met Lys Asp Cys
 1               5                   10                  15
Thr Glu Arg Gln
            20
```

<210> 241
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 241

```
Lys Gly Cys Trp Lys Cys Gly Lys Glu Gly His Gln Met Lys Asp Cys
 1               5                   10                  15
Thr Glu Arg Gln
            20
```

<210> 242
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 242

```
His Gln Met Lys Asp Cys Thr Glu Arg Gln Ala Asn Phe Leu Gly Lys
 1               5                   10                  15
Ile Trp Pro Ser
            20
```

<210> 243
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 243

```
His Gln Met Lys Asp Cys Thr Glu Arg Gln Ala Asn Phe Leu Gly Lys
 1               5                   10                  15
```

Ile Trp Pro Ser
20

<210> 244
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 244
His Gln Met Lys Asp Cys Thr Glu Arg Gln Ala Asn Phe Leu Gly Lys
1 5 10 15
Ile Trp Pro Ser
20

<210> 245
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 245
Ala Thr Leu Glu Glu Met Met Thr Ala Cys Gln Gly Val Gly Gly Pro
1 5 10 15
Gly His Lys Ala
20

<210> 246
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 246
Ala Thr Leu Glu Glu Met Met Thr Ala Cys Gln Gly Val Gly Gly Pro
1 5 10 15
Gly His Lys Ala
20

<210> 247
<211> 21
<212> PRT
<213> Human Immunodeficiency Virus

<400> 247
Cys Gln Gly Val Gly Gly Pro Gly His Lys Ala Arg Val Leu Ala Glu
1 5 10 15
Ala Met Ser Gln Val
20

<210> 248

<211> 21
<212> PRT
<213> Human Immunodeficiency Virus

<400> 248
Cys Gln Gly Val Gly Gly Pro Gly His Lys Ala Arg Val Leu Ala Glu
1 5 10 15

Ala Met Ser Gln Val
20

<210> 249
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 249
Met Phe Ser Ala Leu Ser Glu Gly Ala Thr Pro Gln Asp Leu Asn Thr
1 5 10 15
Met Leu Asn Thr
20

<210> 250
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 250
Met Phe Ser Ala Leu Ser Glu Gly Ala Thr Pro Gln Asp Leu Asn Thr
1 5 10 15
Met Leu Asn Thr
20

<210> 251
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 251
Ser Ile Leu Asp Ile Arg Gln Gly Pro Lys Glu Pro Phe Arg Asp Tyr
1 5 10 15
Val Asp Arg Phe
20

<210> 252
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 252
Ser Ile Leu Asp Ile Arg Gln Gly Pro Lys Glu Pro Phe Arg Asp Tyr
1 5 10 15
Val Asp Arg Phe
20

<210> 253
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 253
Glu Pro Phe Arg Asp Tyr Val Asp Arg Phe Tyr Lys Thr Leu Arg Ala
1 5 10 15
Glu Gln Ala Ser

20

<210> 254
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 254
Glu Pro Phe Arg Asp Tyr Val Asp Arg Phe Tyr Lys Thr Leu Arg Ala
1 5 10 15
Glu Gln Ala Ser
20

<210> 255
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 255
Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Thr Ile Leu Lys Ala
1 5 10 15
Leu Gly Pro Ala
20

<210> 256
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 256
Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Thr Ile Leu Lys Ala
1 5 10 15
Leu Gly Pro Ala
20

<210> 257
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 257
Lys Thr Ile Leu Lys Ala Leu Gly Pro Ala Ala Thr Leu Glu Glu Met
1 5 10 15
Met Thr Ala Cys
20

<210> 258
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 258
Lys Thr Ile Leu Lys Ala Leu Gly Pro Ala Ala Thr Leu Glu Glu Met
1 5 10 15
Met Thr Ala Cys
20

<210> 259
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 259
Lys Thr Ile Leu Lys Ala Leu Gly Pro Ala Ala Thr Leu Glu Glu Met
1 5 10 15
Met Thr Ala Cys
20

<210> 260
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 260
Met Gly Ala Arg Ala Ser Val Leu Ser Gly Gly Glu Leu Asp Arg Trp
1 5 10 15
Glu Lys Ile Arg
20

<210> 261
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 261
Met Gly Ala Arg Ala Ser Val Leu Ser Gly Gly Glu Leu Asp Arg Trp
1 5 10 15
Glu Lys Ile Arg
20

<210> 262
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 262
Gly Glu Leu Asp Arg Trp Glu Lys Ile Arg Leu Arg Pro Gly Gly Lys
1 5 10 15
Lys Lys Tyr Lys
20

<210> 263
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 263
Gly Glu Leu Asp Arg Trp Glu Lys Ile Arg Leu Arg Pro Gly Gly Lys
1 5 10 15
Lys Lys Tyr Lys
20

<210> 264
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 264
Leu Arg Pro Gly Gly Lys Lys Lys Tyr Lys Leu Lys His Ile Val Trp
1 5 10 15
Ala Ser Arg Glu
20

<210> 265
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 265
Leu Arg Pro Gly Gly Lys Lys Lys Tyr Lys Leu Lys His Ile Val Trp
1 5 10 15
Ala Ser Arg Glu
20

<210> 266
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 266
Leu Lys His Ile Val Trp Ala Ser Arg Glu Leu Glu Arg Phe Ala Val
1 5 10 15
Asn Pro Gly Leu
20

<210> 267
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 267
Leu Lys His Ile Val Trp Ala Ser Arg Glu Leu Glu Arg Phe Ala Val
1 5 10 15
Asn Pro Gly Leu
20

<210> 268
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 268
Leu Glu Arg Phe Ala Val Asn Pro Gly Leu Leu Glu Thr Ser Glu Gly
1 5 10 15
Cys Arg Gln Ile
20

<210> 269
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 269
Leu Glu Arg Phe Ala Val Asn Pro Gly Leu Leu Glu Thr Ser Glu Gly
1 5 10 15
Cys Arg Gln Ile
20

<210> 270
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 270
Leu Glu Thr Ser Glu Gly Cys Arg Gln Ile Leu Gly Gln Leu Gln Pro
1 5 10 15
Ser Leu Gln Thr
20

<210> 271
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 271
Leu Glu Thr Ser Glu Gly Cys Arg Gln Ile Leu Gly Gln Leu Gln Pro
1 5 10 15
Ser Leu Gln Thr
20

<210> 272
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 272
Leu Gly Gln Leu Gln Pro Ser Leu Gln Thr Gly Ser Glu Glu Leu Arg
1 5 10 15
Ser Leu Tyr Asn
20

<210> 273
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 273
Leu Gly Gln Leu Gln Pro Ser Leu Gln Thr Gly Ser Glu Glu Leu Arg
1 5 10 15
Ser Leu Tyr Asn
20

<210> 274
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 274
Gly Ser Glu Glu Leu Arg Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr
1 5 10 15
Cys Val His Gln
20

<210> 275
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 275
Gly Ser Glu Glu Leu Arg Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr
1 5 10 15
Cys Val His Gln
20

<210> 276
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 276
Thr Val Ala Thr Leu Tyr Cys Val His Gln Arg Ile Glu Ile Lys Asp
1 5 10 15
Thr Lys Glu Ala
20

<210> 277
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 277
Thr Val Ala Thr Leu Tyr Cys Val His Gln Arg Ile Glu Ile Lys Asp
1 5 10 15
Thr Lys Glu Ala
20

<210> 278
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 278
Arg Ile Glu Ile Lys Asp Thr Lys Glu Ala Leu Asp Lys Ile Glu Glu
1 5 10 15
Glu Gln Asn Lys
20

<210> 279

<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 279
Arg Ile Glu Ile Lys Asp Thr Lys Glu Ala Leu Asp Lys Ile Glu Glu
1 5 10 15
Glu Gln Asn Lys
20

<210> 280
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 280
Leu Asp Lys Ile Glu Glu Glu Gln Asn Lys Ser Lys Lys Lys Ala Gln
1 5 10 15
Gln Ala Ala Ala
20

<210> 281
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 281
Leu Asp Lys Ile Glu Glu Glu Gln Asn Lys Ser Lys Lys Lys Ala Gln
1 5 10 15
Gln Ala Ala Ala
20

<210> 282
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 282
Ser Lys Lys Lys Ala Gln Gln Ala Ala Ala Asp Thr Gly His Ser Asn
1 5 10 15
Gln Val Ser Gln
20

<210> 283
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 283
Ser Lys Lys Lys Ala Gln Gln Ala Ala Ala Asp Thr Gly His Ser Asn
1 5 10 15
Gln Val Ser Gln
20

<210> 284
<211> 20

<212> PRT
<213> Human Immunodeficiency Virus

<400> 284
Asp Thr Gly His Ser Asn Gln Val Ser Gln Asn Tyr Pro Ile Val Gln
1 5 10 15
Asn Ile Gln Gly
20

<210> 285
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 285
Asp Thr Gly His Ser Asn Gln Val Ser Gln Asn Tyr Pro Ile Val Gln
1 5 10 15
Asn Ile Gln Gly
20

<210> 286
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 286
Asn Tyr Pro Ile Val Gln Asn Ile Gln Gly Gln Met Val His Gln Ala
1 5 10 15
Ile Ser Pro Arg
20

<210> 287
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 287
Asn Tyr Pro Ile Val Gln Asn Ile Gln Gly Gln Met Val His Gln Ala
1 5 10 15
Ile Ser Pro Arg
20

<210> 288
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 288
Gln Met Val His Gln Ala Ile Ser Pro Arg Thr Leu Asn Ala Trp Val
1 5 10 15
Lys Val Val Glu
20

<210> 289
<211> 20
<212> PRT

<213> Human Immunodeficiency Virus

<400> 289
Gln Met Val His Gln Ala Ile Ser Pro Arg Thr Leu Asn Ala Trp Val
1 5 10 15
Lys Val Val Glu
20

<210> 290
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 290
Thr Leu Asn Ala Trp Val Lys Val Val Glu Glu Lys Ala Phe Ser Pro
1 5 10 15
Glu Val Ile Pro
20

<210> 291
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 291
Thr Leu Asn Ala Trp Val Lys Val Val Glu Glu Lys Ala Phe Ser Pro
1 5 10 15
Glu Val Ile Pro
20

<210> 292
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 292
Glu Lys Ala Phe Ser Pro Glu Val Ile Pro Met Phe Ser Ala Leu Ser
1 5 10 15
Glu Gly Ala Thr
20

<210> 293
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 293
Glu Lys Ala Phe Ser Pro Glu Val Ile Pro Met Phe Ser Ala Leu Ser
1 5 10 15
Glu Gly Ala Thr
20

<210> 294
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 294
Val Gly Gly His Gln Ala Ala Met Gln Met Leu Lys Glu Thr Ile Asn
1 5 10 15
Glu Glu Ala Ala
20

<210> 295
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 295
Val Gly Gly His Gln Ala Ala Met Gln Met Leu Lys Glu Thr Ile Asn
1 5 10 15
Glu Glu Ala Ala
20

<210> 296
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 296
Leu Lys Glu Thr Ile Asn Glu Glu Ala Ala Glu Trp Asp Arg Val His
1 5 10 15
Pro Val His Ala
20

<210> 297
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 297
Leu Lys Glu Thr Ile Asn Glu Glu Ala Ala Glu Trp Asp Arg Val His
1 5 10 15
Pro Val His Ala
20

<210> 298
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 298
Glu Trp Asp Arg Val His Pro Val His Ala Gly Pro Ile Ala Pro Gly
1 5 10 15
Gln Met Arg Glu
20

<210> 299
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 299
Glu Trp Asp Arg Val His Pro Val His Ala Gly Pro Ile Ala Pro Gly
1 5 10 15
Gln Met Arg Glu
20

<210> 300
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 300
Pro Arg Gly Ser Asp Ile Ala Gly Thr Thr Ser Thr Leu Gln Glu Gln
1 5 10 15
Ile Gly Trp Met
20

<210> 301
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 301
Pro Arg Gly Ser Asp Ile Ala Gly Thr Thr Ser Thr Leu Gln Glu Gln
1 5 10 15
Ile Gly Trp Met
20

<210> 302
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 302
Ser Thr Leu Gln Glu Gln Ile Gly Trp Met Thr Asn Asn Pro Pro Ile
1 5 10 15
Pro Val Gly Glu
20

<210> 303
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 303
Ser Thr Leu Gln Glu Gln Ile Gly Trp Met Thr Asn Asn Pro Pro Ile
1 5 10 15
Pro Val Gly Glu
20

<210> 304
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 304

Thr Asn Asn Pro Pro Ile Pro Val Gly Glu Ile Tyr Lys Arg Trp Ile
1 5 10 15
Ile Leu Gly Leu
20

<210> 305
<211> 20
<212> PRT

<213> Human Immunodeficiency Virus

<400> 305
Thr Asn Asn Pro Pro Ile Pro Val Gly Glu Ile Tyr Lys Arg Trp Ile
1 5 10 15
Ile Leu Gly Leu
20

<210> 306
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 306
Ile Tyr Lys Arg Trp Ile Ile Leu Gly Leu Asn Lys Ile Val Arg Met
1 5 10 15
Tyr Ser Pro Thr
20

<210> 307
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 307
Ile Tyr Lys Arg Trp Ile Ile Leu Gly Leu Asn Lys Ile Val Arg Met
1 5 10 15
Tyr Ser Pro Thr
20

<210> 308
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 308
Asn Lys Ile Val Arg Met Tyr Ser Pro Thr Ser Ile Leu Asp Ile Arg
1 5 10 15
Gln Gly Pro Lys
20

<210> 309
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 309

Asn Lys Ile Val Arg Met Tyr Ser Pro Thr Ser Ile Leu Asp Ile Arg
1 5 10 15
Gln Gly Pro Lys
20

<210> 310
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 310
Tyr Lys Thr Leu Arg Ala Glu Gln Ala Ser Gln Glu Val Lys Asn Trp
1 5 10 15
Met Thr Glu Thr
20

<210> 311
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 311
Tyr Lys Thr Leu Arg Ala Glu Gln Ala Ser Gln Glu Val Lys Asn Trp
1 5 10 15
Met Thr Glu Thr
20

<210> 312
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 312
Gln Glu Val Lys Asn Trp Met Thr Glu Thr Leu Leu Val Gln Asn Ala
1 5 10 15
Asn Pro Asp Cys
20

<210> 313
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 313
Gln Glu Val Lys Asn Trp Met Thr Glu Thr Leu Leu Val Gln Asn Ala
1 5 10 15
Asn Pro Asp Cys
20

<210> 314
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 314
Arg Val Leu Ala Glu Ala Met Ser Gln Val Thr Asn Ser Ala Thr

1 5 10 15

<210> 315
<211> 15
<212> PRT
<213> Human Immunodeficiency Virus

<400> 315
Arg Val Leu Ala Glu Ala Met Ser Gln Val Thr Asn Ser Ala Thr
1 5 10 15

<210> 316
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 316
Thr Asn Ser Ala Thr Ile Met Met Gln Arg Gly Asn Phe Arg Asn Gln
1 5 10 15
Arg Lys Ile Val
20

<210> 317
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 317
Thr Asn Ser Ala Thr Ile Met Met Gln Arg Gly Asn Phe Arg Asn Gln
1 5 10 15
Arg Lys Ile Val
20

<210> 318
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 318
Gly Asn Phe Arg Asn Gln Arg Lys Ile Val Lys Cys Phe Asn Cys Gly
1 5 10 15
Lys Glu Gly His
20

<210> 319
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 319
Gly Asn Phe Arg Asn Gln Arg Lys Ile Val Lys Cys Phe Asn Cys Gly
1 5 10 15
Lys Glu Gly His
20

<210> 320
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 320
Lys Cys Phe Asn Cys Gly Lys Glu Gly His Thr Ala Arg Asn Cys Arg
1 5 10 15
Ala Pro Arg Lys
20

<210> 321
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 321
Lys Cys Phe Asn Cys Gly Lys Glu Gly His Thr Ala Arg Asn Cys Arg
1 5 10 15
Ala Pro Arg Lys
20

<210> 322
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 322
Thr Ala Arg Asn Cys Arg Ala Pro Arg Lys Lys Gly Cys Trp Lys Cys
1 5 10 15
Gly Lys Glu Gly
20

<210> 323
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 323
Thr Ala Arg Asn Cys Arg Ala Pro Arg Lys Lys Gly Cys Trp Lys Cys
1 5 10 15
Gly Lys Glu Gly
20

<210> 324
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 324
Ala Asn Phe Leu Gly Lys Ile Trp Pro Ser Tyr Lys Gly Arg Pro Gly
1 5 10 15
Asn Phe Leu Gln
20

<210> 325

<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 325
Ala Asn Phe Leu Gly Lys Ile Trp Pro Ser Tyr Lys Gly Arg Pro Gly
1 5 10 15
Asn Phe Leu Gln
20

<210> 326
<211> 18
<212> PRT
<213> Human Immunodeficiency Virus

<400> 326
Tyr Lys Gly Arg Pro Gly Asn Phe Leu Gln Ser Arg Pro Glu Pro Thr
1 5 10 15
Ala Pro

<210> 327
<211> 18
<212> PRT
<213> Human Immunodeficiency Virus

<400> 327
Tyr Lys Gly Arg Pro Gly Asn Phe Leu Gln Ser Arg Pro Glu Pro Thr
1 5 10 15
Ala Pro

<210> 328
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 328
Ser Arg Pro Glu Pro Thr Ala Pro Pro Glu Glu Ser Phe Arg Ser Gly
1 5 10 15
Val Glu Thr Thr
20

<210> 329
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 329
Ser Arg Pro Glu Pro Thr Ala Pro Pro Glu Glu Ser Phe Arg Ser Gly
1 5 10 15
Val Glu Thr Thr
20

<210> 330
<211> 21

<212> PRT
<213> Human Immunodeficiency Virus

<400> 330
Pro Glu Glu Ser Phe Arg Ser Gly Val Glu Thr Thr Thr Pro Pro Gln
1 5 10 15
Lys Gln Glu Pro Ile
20

<210> 331
<211> 21
<212> PRT
<213> Human Immunodeficiency Virus

<400> 331
Pro Glu Glu Ser Phe Arg Ser Gly Val Glu Thr Thr Thr Pro Pro Gln
1 5 10 15
Lys Gln Glu Pro Ile
20

<210> 332
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 332
Thr Thr Pro Pro Gln Lys Gln Glu Pro Ile Asp Lys Glu Leu Tyr Pro
1 5 10 15
Leu Thr Ser Leu
20

<210> 333
<211> 20
<212> PRT
<213> Human Immunodeficiency Virus

<400> 333
Thr Thr Pro Pro Gln Lys Gln Glu Pro Ile Asp Lys Glu Leu Tyr Pro
1 5 10 15
Leu Thr Ser Leu
20

<210> 334
<211> 21
<212> PRT
<213> Human Immunodeficiency Virus

<400> 334
Asp Lys Glu Leu Tyr Pro Leu Thr Ser Leu Arg Ser Leu Phe Gly Asn
1 5 10 15
Asp Pro Ser Ser Gln
20

<210> 335
<211> 21
<212> PRT

<213> Human Immunodeficiency Virus

<400> 335
Asp Lys Glu Leu Tyr Pro Leu Thr Ser Leu Arg Ser Leu Phe Gly Asn
1 5 10 15
Asp Pro Ser Ser Gln
20

<210> 336
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 336
Ala Thr Glu Thr Leu Ala Gly Ala Trp Gly Asp Leu Trp Glu Thr Leu
1 5 10 15
Arg Arg Gly Gly
20

<210> 337
<211> 20
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 337
Asp Leu Trp Glu Thr Leu Arg Arg Gly Gly Arg Trp Ile Leu Ala Ile
1 5 10 15
Pro Arg Arg Ile
20

<210> 338
<211> 19
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 338
Arg Trp Ile Leu Ala Ile Pro Arg Arg Ile Arg Gln Gly Leu Glu Leu
1 5 10 15
Thr Leu Leu

<210> 339
<211> 500
<212> PRT
<213> Human Immunodeficiency Virus

<400> 339
Met Gly Ala Arg Ala Ser Val Leu Ser Gly Gly Glu Leu Asp Arg Trp
1 5 10 15
Glu Lys Ile Arg Leu Arg Pro Gly Gly Lys Lys Lys Tyr Lys Leu Lys
20 25 30
His Ile Val Trp Ala Ser Arg Glu Leu Glu Arg Phe Ala Val Asn Pro
35 40 45
Gly Leu Leu Glu Thr Ser Glu Gly Cys Arg Gln Ile Leu Gly Gln Leu
50 55 60
Gln Pro Ser Leu Gln Thr Gly Ser Glu Glu Leu Arg Ser Leu Tyr Asn
65 70 75 80

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Thr Val Ala Thr Leu Tyr Cys Val His Gln Arg Ile Glu Ile Lys Asp
                85                  90                  95
Thr Lys Glu Ala Leu Asp Lys Ile Glu Glu Glu Gln Asn Lys Ser Lys
            100                 105                 110
Lys Lys Ala Gln Gln Ala Ala Ala Asp Thr Gly His Ser Asn Gln Val
        115                 120                 125
Ser Gln Asn Tyr Pro Ile Val Gln Asn Ile Gln Gly Gln Met Val His
    130                 135                 140
Gln Ala Ile Ser Pro Arg Thr Leu Asn Ala Trp Val Lys Val Val Glu
145                 150                 155                 160
Glu Lys Ala Phe Ser Pro Glu Val Ile Pro Met Phe Ser Ala Leu Ser
                165                 170                 175
Glu Gly Ala Thr Pro Gln Asp Leu Asn Thr Met Leu Asn Thr Val Gly
            180                 185                 190
Gly His Gln Ala Ala Met Gln Met Leu Lys Glu Thr Ile Asn Glu Glu
        195                 200                 205
Ala Ala Glu Trp Asp Arg Val His Pro Val His Ala Gly Pro Ile Ala
    210                 215                 220
Pro Gly Gln Met Arg Glu Pro Arg Gly Ser Asp Ile Ala Gly Thr Thr
225                 230                 235                 240
Ser Thr Leu Gln Glu Gln Ile Gly Trp Met Thr Asn Asn Pro Pro Ile
                245                 250                 255
Pro Val Gly Glu Ile Tyr Lys Arg Trp Ile Ile Leu Gly Leu Asn Lys
            260                 265                 270
Ile Val Arg Met Tyr Ser Pro Thr Ser Ile Leu Asp Ile Arg Gln Gly
        275                 280                 285
Pro Lys Glu Pro Phe Arg Asp Tyr Val Asp Arg Phe Tyr Lys Thr Leu
    290                 295                 300
Arg Ala Glu Gln Ala Ser Gln Glu Val Lys Asn Trp Met Thr Glu Thr
305                 310                 315                 320
Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Thr Ile Leu Lys Ala
                325                 330                 335
Leu Gly Pro Ala Ala Thr Leu Glu Glu Met Met Thr Ala Cys Gln Gly
            340                 345                 350
Val Gly Gly Pro Gly His Lys Ala Arg Val Leu Ala Glu Ala Met Ser
        355                 360                 365
Gln Val Thr Asn Ser Ala Thr Ile Met Met Gln Arg Gly Asn Phe Arg
    370                 375                 380
Asn Gln Arg Lys Ile Val Lys Cys Phe Asn Cys Gly Lys Glu Gly His
385                 390                 395                 400
Thr Ala Arg Asn Cys Arg Ala Pro Arg Lys Lys Gly Cys Trp Lys Cys
                405                 410                 415
Gly Lys Glu Gly His Gln Met Lys Asp Cys Thr Glu Arg Gln Ala Asn
            420                 425                 430
Phe Leu Gly Lys Ile Trp Pro Ser Tyr Lys Gly Arg Pro Gly Asn Phe
        435                 440                 445
Leu Gln Ser Arg Pro Glu Pro Thr Ala Pro Pro Glu Glu Ser Phe Arg
    450                 455                 460
Ser Gly Val Glu Thr Thr Thr Pro Pro Gln Lys Gln Glu Pro Ile Asp
465                 470                 475                 480
Lys Glu Leu Tyr Pro Leu Thr Ser Leu Arg Ser Leu Phe Gly Asn Asp
                485                 490                 495
Pro Ser Ser Gln
            500
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<210> 340
<211> 879
<212> PRT
<213> Simian Immunodeficiency Virus

<400> 340

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Met Gly Cys Leu Gly Asn Gln Leu Leu Ile Ala Ile Leu Leu Leu Ser
 1               5                  10                  15
Val Tyr Gly Thr Tyr Cys Thr Leu Tyr Val Thr Val Phe Tyr Gly Val
            20                  25                  30
Pro Ala Trp Arg Asn Ala Thr Ile Pro Leu Phe Cys Ala Thr Lys Asn
        35                  40                  45
Arg Asp Thr Trp Gly Thr Thr Gln Cys Leu Pro Asp Asn Gly Asp Tyr
    50                  55                  60
Ser Glu Leu Ala Leu Asn Val Thr Glu Ser Phe Asp Ala Trp Asn Asn
65                  70                  75                  80
Thr Val Thr Glu Gln Ala Ile Glu Asp Val Trp Gln Leu Phe Glu Thr
                85                  90                  95
Ser Ile Lys Pro Cys Val Lys Leu Ser Pro Leu Cys Ile Thr Met Arg
            100                 105                 110
Cys Asn Lys Ser Glu Thr Asp Arg Trp Gly Leu Thr Lys Ser Ile Thr
        115                 120                 125
Thr Thr Ala Ser Thr Thr Ser Thr Thr Ala Ser Ala Lys Val Asp Met
    130                 135                 140
Val Asn Glu Thr Ser Ser Cys Ile Ala Gln Asp Asn Cys Thr Gly Leu
145                 150                 155                 160
Glu Gln Glu Gln Met Ile Ser Cys Lys Phe Asn Met Thr Gly Leu Lys
                165                 170                 175
Arg Asp Lys Lys Lys Glu Tyr Asn Glu Thr Trp Tyr Ser Ala Asp Leu
            180                 185                 190
Val Cys Glu Gln Gly Asn Ser Thr Gly Asn Glu Ser Arg Cys Tyr Met
        195                 200                 205
Asn His Cys Asn Thr Ser Val Ile Gln Glu Ser Cys Asp Lys His Tyr
    210                 215                 220
Trp Asp Ala Ile Arg Phe Arg Tyr Cys Ala Pro Pro Gly Tyr Ala Leu
225                 230                 235                 240
Leu Arg Cys Asn Asp Thr Asn Tyr Ser Gly Phe Met Pro Lys Cys Ser
                245                 250                 255
Lys Val Val Val Ser Ser Cys Thr Arg Met Met Glu Thr Gln Thr Ser
            260                 265                 270
Thr Trp Phe Gly Phe Asn Gly Thr Arg Ala Glu Asn Arg Thr Tyr Ile
        275                 280                 285
Tyr Trp His Gly Lys Asp Asn Arg Thr Ile Ile Ser Leu Asn Lys Tyr
    290                 295                 300
Tyr Asn Leu Thr Ile Lys Cys Arg Arg Pro Gly Asn Lys Thr Val Leu
305                 310                 315                 320
Pro Val Thr Ile Met Ser Gly Leu Val Phe His Ser Gln Pro Ile Asn
                325                 330                 335
Asp Arg Pro Lys Gln Ala Trp Cys Trp Phe Gly Gly Lys Trp Lys Asp
            340                 345                 350
Ala Ile Lys Glu Val Lys Gln Thr Ile Val Lys His Pro Arg Tyr Thr
        355                 360                 365
Gly Thr Asn Asp Thr Ala Arg Ile Asn Leu Thr Ala Pro Gly Gly Gly
    370                 375                 380
Asp Pro Glu Val Thr Phe Met Trp Thr Asn Cys Arg Gly Glu Phe Leu
385                 390                 395                 400
Tyr Cys Lys Met Asn Trp Phe Leu Asn Trp Val Glu Asp Arg Asn Thr
                405                 410                 415
Thr Asn Gln Lys Pro Lys Glu Gln Tyr Lys Arg Asn Tyr Val Pro Cys
            420                 425                 430
His Ile Arg Gln Ile Ile Asn Thr Trp His Lys Val Gly Lys Asn Val
        435                 440                 445
Tyr Leu Pro Pro Arg Glu Gly Asp Leu Thr Cys Asn Ser Thr Val Thr
    450                 455                 460
Ser Leu Ile Ala Asn Ile Asp Trp Ile Asp Gly Asn Gln Thr Asn Ile
465                 470                 475                 480
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Thr Met Ser Ala Glu Val Ala Glu Leu Tyr Arg Leu Glu Leu Gly Asp
                485                 490                 495
Tyr Lys Leu Val Glu Ile Thr Pro Ile Gly Leu Ala Pro Thr Asn Val
            500                 505                 510
Lys Arg Tyr Thr Thr Gly Gly Thr Ser Arg Asn Lys Arg Gly Val Phe
        515                 520                 525
Val Leu Gly Phe Leu Gly Phe Leu Ala Thr Ala Gly Ser Ala Met Gly
    530                 535                 540
Ala Ala Ser Leu Thr Leu Thr Ala Gln Ser Arg Thr Leu Leu Ala Gly
545                 550                 555                 560
Ile Val Gln Gln Gln Gln Gln Leu Leu Asp Val Val Lys Arg Gln Gln
                565                 570                 575
Glu Leu Leu Arg Leu Thr Val Trp Gly Thr Lys Asn Leu Gln Thr Arg
            580                 585                 590
Val Thr Ala Ile Glu Lys Tyr Leu Lys Asp Gln Ala Gln Leu Asn Ala
        595                 600                 605
Trp Gly Cys Ala Phe Arg Gln Val Cys His Thr Thr Val Pro Trp Pro
    610                 615                 620
Asn Thr Ser Leu Thr Pro Lys Trp Asp Asn Glu Thr Trp Gln Glu Trp
625                 630                 635                 640
Glu Arg Lys Val Asp Phe Leu Glu Glu Asn Ile Thr Ala Leu Pro Glu
                645                 650                 655
Glu Ala Gln Ile Gln Gln Glu Lys Asn Met Tyr Glu Leu Gln Lys Leu
            660                 665                 670
Asn Ser Trp Asp Val Phe Gly Asn Trp Phe Asp Leu Ala Ser Trp Ile
        675                 680                 685
Lys Tyr Ile Gln Tyr Gly Val Tyr Ile Val Val Gly Val Ile Leu Leu
    690                 695                 700
Arg Ile Val Ile Tyr Ile Val Gln Met Leu Ala Lys Leu Arg Gln Gly
705                 710                 715                 720
Tyr Arg Pro Val Phe Ser Ser Pro Pro Ser Tyr Phe Gln Gln Thr His
                725                 730                 735
Ile Gln Gln Asp Pro Ala Leu Pro Thr Arg Glu Gly Lys Glu Gly Asp
            740                 745                 750
Gly Gly Glu Gly Asp Gly Asn Ser Ser Trp Pro Trp Gln Ile Glu Tyr
        755                 760                 765
Ile His Leu Leu Ile Arg Gln Leu Ile Arg Leu Leu Thr Trp Leu Phe
    770                 775                 780
Ser Asn Cys Arg Thr Leu Leu Ser Arg Val Tyr Gln Ile Leu Gln Pro
785                 790                 795                 800
Ile Leu Gln Arg Leu Ser Ala Thr Leu Gln Arg Ile Arg Glu Val Leu
                805                 810                 815
Arg Thr Glu Leu Thr Tyr Leu Gln Tyr Gly Trp Ser Tyr Phe His Glu
            820                 825                 830
Ala Val Gln Ala Ala Trp Arg Ser Ala Thr Glu Thr Leu Ala Gly Ala
        835                 840                 845
Trp Gly Asp Leu Trp Glu Thr Leu Arg Arg Gly Gly Arg Trp Ile Leu
    850                 855                 860
Ala Ile Pro Arg Arg Ile Arg Gln Gly Leu Glu Leu Thr Leu Leu
865                 870                 875
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